

SearchSTN

Welcome to STN International! Enter x:x

LOGINID:sseptal612bxx

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

***** Welcome to STN International *****

NEWS 1 Web Page for STN Seminar Schedule - N. America
NEWS 2 JAN 02 STN pricing information for 2008 now available
NEWS 3 JAN 16 CAS patent coverage enhanced to include exemplified
prophetic substances
NEWS 4 JAN 28 USPATFULL, USPAT2, and USPATOLD enhanced with new
custom IPC display formats
NEWS 5 JAN 28 MARPAT searching enhanced
NEWS 6 JAN 28 USGENE now provides USPTO sequence data within 3 days
of publication
NEWS 7 JAN 28 TOXCENTER enhanced with reloaded MEDLINE segment
NEWS 8 JAN 28 MEDLINE and LMEEDLINE reloaded with enhancements
NEWS 9 FEB 08 STN Express, Version 8.3, now available
NEWS 10 FEB 20 PCI now available as a replacement to DPCI
NEWS 11 FEB 25 IFIREF reloaded with enhancements
NEWS 12 FEB 25 IMSPRODUCT reloaded with enhancements
NEWS 13 FEB 29 WPINDEX/WPIDS/WPIX enhanced with ECLA and current
U.S. National Patent Classification
NEWS 14 MAR 31 IFICDB, IFIPAT, and IFIUDB enhanced with new custom
IPC display formats
NEWS 15 MAR 31 CAS REGISTRY enhanced with additional experimental
spectra
NEWS 16 MAR 31 CA/CAPLUS and CASREACT patent number format for U.S.
applications updated
NEWS 17 MAR 31 LPCI now available as a replacement to LDPCI
NEWS 18 MAR 31 EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS 19 APR 04 STN AnaVist, Version 1, to be discontinued
NEWS 20 APR 15 WPIDS, WPINDEX, and WPIX enhanced with new
predefined hit display formats
NEWS 21 APR 28 EMBASE Controlled Term thesaurus enhanced
NEWS 22 APR 28 IMSRESEARCH reloaded with enhancements
NEWS 23 MAY 30 INPAFAMDB now available on STN for patent family
searching
NEWS 24 MAY 30 DGENE, PCTGEN, and USGENE enhanced with new homology
sequence search option
NEWS 25 JUN 06 EPFULL enhanced with 260,000 English abstracts
NEWS 26 JUN 06 KOREAPAT updated with 41,000 documents
NEWS 27 JUN 13 USPATFULL and USPAT2 updated with 11-character
patent numbers for U.S. applications
NEWS 28 JUN 19 CAS REGISTRY includes selected substances from
web-based collections

NEWS EXPRESS FEBRUARY 08 CURRENT WINDOWS VERSION IS V8.3,

Updated Search

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AND CURRENT DISCOVER FILE IS DATED 20 FEBRUARY 2008

NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS LOGIN Welcome Banner and News Items
NEWS IPC8 For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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***** STN Columbus *****

FILE 'HOME' ENTERED AT 13:57:46 ON 22 JUN 2008

=>

Uploading

THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE

Do you want to switch to the Registry File?

Choice (Y/n):

Switching to the Registry File...

Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> FILE REGISTRY

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	1.68	1.68

FILE 'REGISTRY' ENTERED AT 14:02:26 ON 22 JUN 2008

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STRUCTURE FILE UPDATES: 20 JUN 2008 HIGHEST RN 1029712-63-7

DICTIONARY FILE UPDATES: 20 JUN 2008 HIGHEST RN 1029712-63-7

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TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of

Updated Search

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experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stdoc/properties.html>

=>

Uploading C:\Documents and Settings\brobinson1\My Documents\stnweb\Queries\drt.str

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 14:09:54 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 726 TO ITERATE

100.0% PROCESSED 726 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 12904 TO 16136

PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 full

THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 177.90 U.S. DOLLARS

DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y

FULL SEARCH INITIATED 14:09:59 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 13884 TO ITERATE

100.0% PROCESSED 13884 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.01

L3 2 SEA SSS FUL L1

=> file hcaplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

183.88

185.56

FILE 'HCAPLUS' ENTERED AT 14:10:02 ON 22 JUN 2008

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FILE COVERS 1907 - 22 Jun 2008 VOL 148 ISS 26

FILE LAST UPDATED: 20 Jun 2008 (20080620/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3

L4 1 L3

=> d l4, ibib abs hitstr, 1

L4 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:540564 HCAPLUS

DOCUMENT NUMBER: 143:77864

TITLE: Urea-based peptidomimetics as somatostatin receptor subtype 1 (SSTR1) modulators, their preparation and use in therapy

INVENTOR(S): Knuuttila, Pia; Salo, Harri; Tomperi, Jussi; Wurster, Siegfried; Hoffren, Anna-Marja

PATENT ASSIGNEE(S): Oy Juvantia Pharma Ltd., Finland

SOURCE: PCT Int. Appl., 58 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005056520	A1	20050623	WO 2004-FI750	20041209
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2547863	A1	20050623	CA 2004-2547863	20041209
EP 1692099	A1	20060823	EP 2004-805145	20041209
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
JP 2007513928	T	20070531	JP 2006-543564	20041209

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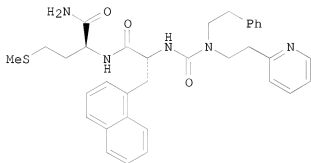
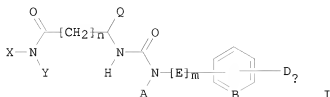
PRIORITY APPLN. INFO.:

FI 2003-1824
US 2003-509073P
WO 2004-FI750

A 20031212
P 20031212
W 20041209

OTHER SOURCE(S):
GI

CASREACT 143:77864; MARPAT 143:77864



AB The invention relates to a group of novel urea-based peptidomimetics I, which are modulators of somatostatin receptor subtype 1 (SSTR1). In compds. I, X is H, (un)substituted aryl, (un)substituted heteroaryl, etc.; Y is H, C1-6 alkyl, C3-7 cycloalkyl, or C3-7 cycloalkyl-C1-3 alkyl; Q is aryl, aryl-C1-6 alkyl, heteroaryl, or heteroaryl-C1-6 alkyl, where aryl and heteroaryl are optionally substituted with one to three substituents and alkyl is optionally substituted with cycloalkyl, heterocyclyl, aryl, or heteroaryl; A is (un)substituted C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, (un)substituted cycloalkyl, (un)substituted heterocyclyl, (un)substituted aryl, or (un)substituted heteroaryl; B is N or C (with D attached); D is independently selected from H, halo, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, amino, NO₂, or cyano; E is (un)substituted C; h is 0-4; n is 0 or 1; and m is 0-3; provided that A is not 2-hydroxyethyl, and with 1 specific exclusion. The invention also relates to the preparation of I, pharmaceutical compns. containing I as an active ingredient with at least one pharmaceutically acceptable carrier, as well as to the use of I for the treatment or prevention of diseases or conditions involving SSTR1. Rink amide resin was washed and coupled with N-Fmoc-L-methionine followed by removal of the Fmoc protecting group, coupling with Fmoc-3-naphthalen-1-yl-D-alanine [i.e., (R)-2-(Fmoc-amino)-3-(naphth-1-yl)-propanoic acid], and deprotection. The resulting amine underwent acylation with 4-nitrophenyl chloroformate followed by substitution with phenethyl(2-pyridin-2-

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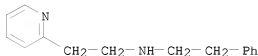
ylethyl)amine (preparation given) and cleavage from the resin to give urea-based peptidomimetic II. The compds. of the invention are selective for SSTR1 and SSTR4 over SSTR2, SSTR3, and SSTR5, and can therefore be useful in combination with a detectable label for tissue imaging, or as carriers for another therapeutically active compound to be targeted to tissues containing SSTR1. Compound II has a K_i value of 19 nM for SSTR1, 640

nM for SSTR4, and >10,000 nM for SSTR2, SSTR3, and SSTR5. A large set of other compds. of the invention had a K_i value of less than 100 nM for SSTR1.

IT 218144-88-8P, Phenethyl(2-pyridin-2-ylethyl)amine
855308-94-0P, (3-Phenylpropyl)[2-(pyridin-2-yl)ethyl]amine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of urea-based peptidomimetics as somatostatin receptor subtype 1 modulators)

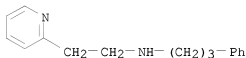
RN 218144-88-8 HCAPLUS

CN 2-Pyridineethanamine, N-(2-phenylethyl)- (CA INDEX NAME)



RN 855308-94-0 HCAPLUS

CN 2-Pyridineethanamine, N-(3-phenylpropyl)- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> file caold

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
	8.14	193.70
FULL ESTIMATED COST		
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
	-0.80	-0.80
CA SUBSCRIBER PRICE		

FILE 'CAOLD' ENTERED AT 14:10:20 ON 22 JUN 2008
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FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

Updated Search

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This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

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This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

=> d his

(FILE 'HOME' ENTERED AT 13:57:46 ON 22 JUN 2008)

FILE 'REGISTRY' ENTERED AT 14:02:26 ON 22 JUN 2008

L1 STRUCTURE UPLOADED

L2 0 S L1

L3 2 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 14:10:02 ON 22 JUN 2008

L4 1 S L3

FILE 'CAOLD' ENTERED AT 14:10:20 ON 22 JUN 2008

=> s l3

L5 0 L3

=> file reg

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	0.46	194.16
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	-0.80

FILE 'REGISTRY' ENTERED AT 14:10:26 ON 22 JUN 2008

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STRUCTURE FILE UPDATES: 20 JUN 2008 HIGHEST RN 1029712-63-7

DICTIONARY FILE UPDATES: 20 JUN 2008 HIGHEST RN 1029712-63-7

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<http://www.cas.org/support/stngen/stdoc/properties.html>

=>

Uploading C:\Documents and Settings\brobinson1\My Documents\stnweb\Queries\34rg.str

L6 STRUCTURE UPLOADED

=> d l6

L6 HAS NO ANSWERS

L6 STR

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.

=> s l6

SAMPLE SEARCH INITIATED 14:12:39 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 601 TO ITERATE

100.0% PROCESSED 601 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 10550 TO 13490

PROJECTED ANSWERS: 0 TO 0

L7 0 SEA SSS SAM L6

=> s l6 full

THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 177.90 U.S. DOLLARS

DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y

FULL SEARCH INITIATED 14:12:43 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 11853 TO ITERATE

100.0% PROCESSED 11853 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

L8 0 SEA SSS FUL L6

=>

Uploading C:\Documents and Settings\brobinson1\My Documents\stnweb\Queries\asdfnjl.str

L9 STRUCTURE UPLOADED

=> d l9

L9 HAS NO ANSWERS

Updated Search

SearchSTN

L9 STR

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.

=> s 19

SAMPLE SEARCH INITIATED 14:13:53 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 726 TO ITERATE

100.0% PROCESSED 726 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**

PROJECTED ITERATIONS: 12904 TO 16136
PROJECTED ANSWERS: 0 TO 0

L10 0 SEA SSS SAM L9

=> s 19 full

THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 177.90 U.S. DOLLARS

DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y

FULL SEARCH INITIATED 14:13:58 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 13884 TO ITERATE

100.0% PROCESSED 13884 ITERATIONS 3 ANSWERS
SEARCH TIME: 00.00.01

L11 3 SEA SSS FUL L9

=> file hcaplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	358.56	552.72

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-0.80

FILE 'HCAPLUS' ENTERED AT 14:14:01 ON 22 JUN 2008

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FILE COVERS 1907 - 22 Jun 2008 VOL 148 ISS 26
FILE LAST UPDATED: 20 Jun 2008 (20080620/ED)

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This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s l11

L12 1 L11

=> file reg

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	2.69	555.41
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	-0.80

FILE 'REGISTRY' ENTERED AT 14:14:11 ON 22 JUN 2008
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experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stdoc/properties.html>

=>

Uploading C:\Documents and Settings\brobinson1\My
Documents\stnweb\Queries\andfhg.str

L13 STRUCTURE UPLOADED

=> d l13

L13 HAS NO ANSWERS
L13 STR

Updated Search

SearchSTN

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> s l13

SAMPLE SEARCH INITIATED 14:16:31 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 726 TO ITERATE

100.0% PROCESSED 726 ITERATIONS

5 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 12904 TO 16136

PROJECTED ANSWERS: 5 TO 234

L14 5 SEA SSS SAM L13

=> s l13 full

THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 177.90 U.S. DOLLARS

DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y

FULL SEARCH INITIATED 14:16:36 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 13884 TO ITERATE

100.0% PROCESSED 13884 ITERATIONS

85 ANSWERS

SEARCH TIME: 00.00.01

L15 85 SEA SSS FUL L13

=> file hcaplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

179.74

735.15

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

0.00

-0.80

FILE 'HCAPLUS' ENTERED AT 14:16:39 ON 22 JUN 2008

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FILE COVERS 1907 - 22 Jun 2008 VOL 148 ISS 26

Updated Search

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FILE LAST UPDATED: 20 Jun 2008 (20080620/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s l15
L16      49 L15

=> s l16 and rode, b?/au
      404 RODE, B?/AU
L17      0 L16 AND RODE, B?/AU

=> s l16 and rozman, d?/au
      70 ROZMAN, D?/AU
L18      0 L16 AND ROZMAN, D?/AU

=> s l16 and tacer, k?/au
      6 TACER, K?/AU
L19      0 L16 AND TACER, K?/AU

=> s l16 and kocjan, d?/au
      73 KOCJAN, D?/AU
L20      0 L16 AND KOCJAN, D?/AU

=> d l16, ibib abs fhitr, 1-49
```

```
L16 ANSWER 1 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1260327 HCAPLUS
DOCUMENT NUMBER: 148:113426
TITLE: Vasculoprotective effects of somatostatin receptor
      subtypes
AUTHOR(S): Tigerstedt, Nina-Maria; Aavik, Einari; Aavik, Silja;
      Savolainen-Peltonen, Hanna; Hayry, Pekka
CORPORATE SOURCE: Rational Drug Design Programme, Biomedicum Helsinki
      and Transplantation Laboratory, University of Helsinki
      and Helsinki University Central Hospital, Helsinki,
      Finland
SOURCE: Molecular and Cellular Endocrinology (2007), 279(1-2),
      34-38
      CODEN: MCEND6; ISSN: 0303-7207
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors have shown that somatostatin agonist peptide CH275, selective
to somatostatin receptor (sst) subtypes 1,4, was more effective in
preventing intimal hyperplasia than the sst2,3,5-selective octreotide,
raising the question what are the sep. roles of the sst1- and 4-subtypes.
Here, the authors dissect this observation further with highly
subtype-selective peptidomimetics and demonstrate that, after rat carotid
denudation, both the sst1- and 4-selective analogs (300 µg/kg/day,
s.c.) increased lumen size, while only the sst4-selective analog
significantly reduced intimal nuclei number, intimal area, and intima/media
ratio. The 2,3,5-selective compds. had no effect on these parameters.
The observed in vivo effects were further investigated ex vivo with explant
```

Updated Search

outgrowth from pieces of vascular wall. The sst4-selective analog was more effective than the sst1-selective one in inhibiting the percent of outgrowth and the migration of cells from the explants while neither compound affected proliferation. Thus, selective targeting to sst4 should be considered when developing orally active vasculoprotective therapies.

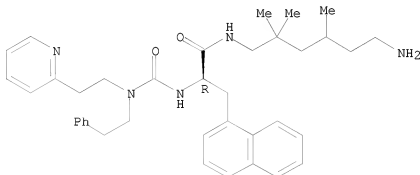
IT 217480-24-5, L 797591

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(somatostatin receptor peptidomimetics effects on intimal hyperplasia following carotid artery denudation in rats)

RN 217480-24-5 HCAPLUS

CN 1-Naphthalenepropanamide, N-(6-amino-2,2,4-trimethylhexyl)- α -[[[(2-phenylethyl)[2-(2-pyridinyl)ethyl]amino]carbonyl]amino]-, (α R)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 2 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:152722 HCAPLUS

DOCUMENT NUMBER: 146:309585

TITLE: Somatostatin, a negative-regulator of central leptin action in the rat hypothalamus

AUTHOR(S): Stepanyan, Z.; Kocharyan, A.; Behrens, M.; Koebrick, C.; Pyrski, M.; Meyerhof, W.

CORPORATE SOURCE: Department of Molecular Genetics, German Institute of Human Nutrition Potsdam-Rehbruecke, Nuthetal, Germany

SOURCE: Journal of Neurochemistry (2007), 100(2), 468-478

CODEN: JONRA9; ISSN: 0022-3042

PUBLISHER: Blackwell Publishing Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

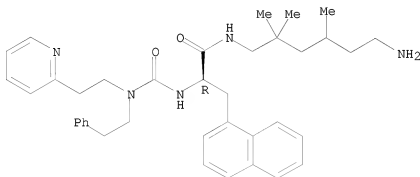
AB Leptin-responsive neurons of the hypothalamus constitute a heterogeneous population expressing a vast array of different neuropeptides and neurotransmitters, some of which participate in the regulation of hunger and satiety. Here we report that somatostatin modulates the efficacy of leptin-signaling in the rat hypothalamus. Using a two-pulse paradigm at 30-min intervals, we delivered somatostatin or somatostatin receptor subtype-selective agonists in combination with leptin into the lateral cerebral ventricle of stereotaxically cannulated rats. To monitor the effect of somatostatin on the leptin-signaling pathway, we quantified

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changes in the leptin-mediated activation of STAT3, the signal transducer and activator of transcription 3. Successive administration of somatostatin and leptin diminished the level of STAT3-phosphorylation and nuclear STAT3 translocation in the ventromedial and dorsomedial hypothalamic nuclei, the lateral hypothalamic area, and the arcuate nucleus by about 40% compared to leptin administration alone. Furthermore, application of subtype-selective somatostatin receptor agonists suggests that the observed reduction in leptin-responsiveness is predominantly mediated by the sst3 receptor-subtype, followed by sst1 and sst2. In addition, the intensity of the neg.-regulatory effect of somatostatin on leptin-signaling displayed regional differences for the three receptor-subtypes involved. Addressing the functional consequences of the diminished leptin-signaling, behavioral analyses showed that centrally applied somatostatin counteracts the leptin-mediated suppression of food intake. These results suggest that the pleiotropic effector somatostatin also plays a role in the central regulation of energy homeostasis.

IT 217480-24-5, L 797591
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (somatostatin as neg.-regulator of central leptin action and signaling
 in rat hypothalamus)
 RN 217480-24-5 HCAPLUS
 CN 1-Naphthalenepropanamide, N-(6-amino-2,2,4-trimethylhexyl)- α -[[[(2-phenylethyl)[2-(2-pyridinyl)ethyl]amino]carbonyl]amino]-, (α R)- (CA
 INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2007:35021 HCAPLUS
 DOCUMENT NUMBER: 146:244639
 TITLE: Porcine somatostatin receptor 2 displays typical pharmacological sst2 features but unique dynamics of homodimerization and internalization
 AUTHOR(S): Duran-Prado, Mario; Bucharles, Christine; Gonzalez, Bruno J.; Vazquez-Martinez, Rafael; Martinez-Fuentes, Antonio J.; Garcia-Navarro, Socorro; Rhodes, Simon J.; Vaudry, Hubert; Malagon, Maria M.; Castano, Justo P.
 CORPORATE SOURCE: Department of Cell Biology, Physiology and Immunology,

Updated Search

SearchSTN

SOURCE: University of Cordoba, Cordoba, E-14014, Spain
Endocrinology (2007), 148(1), 411-421
CODEN: ENDOAO; ISSN: 0013-7227

PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal

LANGUAGE: English

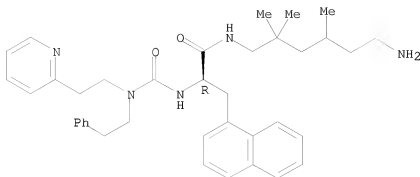
AB Somatostatin (SRIF) exerts its multiple actions, including inhibition of GH secretion and of tumoral growth, through a family of five receptor subtypes (sst1-sst5). We recently reported that an sst2-selective agonist markedly decreases GH release from pig somatotropes, suggesting important roles for this scarcely explored receptor, psst2. Here, functional expression of psst2 in Chinese hamster ovary-K1 and human embryonic kidney-293-AD cell lines was employed to determine its pharmacol. features and functional ability to reduce cAMP, and to examine its homodimerization and internalization dynamics in real time in single living cells. Results show that psst2 is a high-affinity receptor (dissociation constant = 0.27 nM) displaying a typical sst2 profile (nM affinity for SRIF-14≥SRIF-28>cortistatin>MK678>octreotide) and high selectivity (EC50 = 1.1 nM) for the sst2 agonist L-779,976, but millimolar or undetectable affinity to other sst-specific agonists (sst3>sst1>sst5>>sst4). Accordingly, SRIF dose-dependently inhibited forskolin-stimulated cAMP with high potency (EC50 = 6.55 pM) and modest efficacy (maximum 29.1%) via psst2. Cotransfection of human embryonic kidney-293 and Chinese hamster ovary-K1 cells with two receptor constructs modified with distinct fluorescent tags (psst2-YFP/psst2-CFP) enabled fluorescence resonance energy transfer measurement of phys. interaction between psst2 receptors and also receptor internalization in single living cells. This revealed that under basal conditions, psst2 forms constitutive homodimers/homomultimers, which dissociate immediately (11 s) upon SRIF binding. Interestingly, contrary to human sst2, psst2 rapidly reassoci. (110.5 s) during a subsequent process that temporally overlaps with receptor internalization (half-maximal = 95.1 s). Therefore, psst2 is a potent inhibitory receptor displaying a unique set of interrelated dynamic features of agonist-dependent dimerization, dissociation, internalization, and reassoci., a cascade of events that might be critical for receptor function.

IT 217480-24-5, L-797591
RL: BSU (Biological study, unclassified); PKT (Pharmacokinetics); BIOL (Biological study)
(porcine somatostatin receptor 2 displays typical pharmacol. sst2 features but unique dynamics of homodimerization and internalization)

RN 217480-24-5 HCAPLUS

CN 1-Naphthalenepropanamide, N-(6-amino-2,2,4-trimethylhexyl)-α-[[[(2-phenylethyl)[2-(2-pyridinyl)ethyl]amino]carbonyl]amino]-, (αR)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:521302 HCAPLUS

DOCUMENT NUMBER: 144:481339

TITLE: Identification of the somatostatin receptor subtypes (sst) mediating the divergent, stimulatory/inhibitory actions of somatostatin on growth hormone secretion
 AUTHOR(S): Luque, Raul M.; Duran-Prado, Mario; Garcia-Navarro, Socorro; Gracia-Navarro, Francisco; Kineman, Rhonda D.; Malagon, Maria M.; Castano, Justo P.

CORPORATE SOURCE: Department of Cell Biology, Physiology, and Immunology, University of Cordoba, Cordoba, E-14014, Spain

SOURCE: Endocrinology (2006), 147(6), 2902-2908

CODEN: ENDOAO; ISSN: 0013-7227

PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB It is well established that somatostatin acts through G protein-coupled receptors, termed sst, to inhibit GH release. However in pigs somatostatin can stimulate or inhibit in vitro GH secretion in a dose- and somatotroph subpopulation-dependent manner. We report herein that somatostatin-stimulated GH release is blocked by pretreatment with GTPγ-S, suggesting an involvement of G protein-coupled receptors. Consistent with this, an sst5 selective agonist stimulated spontaneous GH secretion at doses ranging 10⁻¹³ to 10⁻⁹ M, without influencing GHRH-induced GH release. Conversely, sst1-, sst2-, sst3-, and sst4-specific agonists inhibited GHRH-evoked GH release but not basal GH secretion. Examination of the effects of sst-specific agonists on two subpopulations of somatotroph cells separated by d. gradient centrifugation [low- (LD) and high-d. (HD) cells] showed that only a low dose of the sst5 agonist stimulated GH release in LD somatotrophs, whereas both low and high doses of this agonist stimulated GH release in HD cells. In marked contrast, sst1 and sst2 agonists blocked GHRH-stimulated GH release in LD cells at all doses tested, whereas only a high dose of the sst2 agonist inhibited GHRH-induced GH release in HD somatotrophs. Interestingly, sst expression pattern in these subpopulations correlates with the distinct actions of sst-selective agonists; specifically, sst5 is more abundant in HD somatotrophs, whereas sst1 and sst2 mRNA predominate in LD cells. These results indicate that in the pig, sst1 and sst2 are the primary

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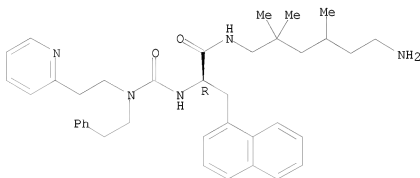
mediators of the inhibitory effects of somatostatin, whereas sst5 or an sst5-related mechanism mediates the stimulatory action of somatostatin on GH release.

IT 217480-24-5, L 797591
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (somatostatin receptor subtypes mediation of divergent stimulatory/inhibitory actions of somatostatin on growth hormone secretion in pig somatotroph type-dependent manner)

RN 217480-24-5 HCAPLUS

CN 1-Naphthalenepropanamide, N-(6-amino-2,2,4-trimethylhexyl)- α -[[[(2-phenylethyl)[2-(2-pyridinyl)ethyl]amino]carbonyl]amino]-, (aR)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 5 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:1345046 HCAPLUS

DOCUMENT NUMBER: 144:69823

TITLE: Preparation of heteroarylpyrazoles as p38 kinase inhibitors

INVENTOR(S): Naraian, Ashok S.; Clare, Michael; Collins, Paul W.; Crich, Joyce Zuowu; Devraj, Rajesh; Flynn, Daniel L.; Geng, Lifeng; Graneto, Matthew J.; Hanau, Cathleen E.; Hanson, Gunnar J.; Hartmann, Susan J.; Hepperle, Michael; Huang, He; Koszyk, Francis J.; Liao, Shuyuan; Metz, Suzanne; Partis, Richard A.; Perry, Thao D.; Rao, Shashidhar N.; Selness, Shaun Raj; South, Michael S.; Stealey, Michael A.; Talley, John Jeffrey; Vazquez, Michael L.; Weier, Richard M.; Xu, Xiangdong; Khanna, Ish K.; Yu, Yi; Naing, Win; Walker, John; Yang, Syaulan

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: U.S., 548 pp.
 CODEN: USXXAM

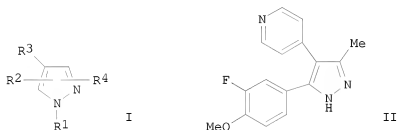
DOCUMENT TYPE: Patent
 LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

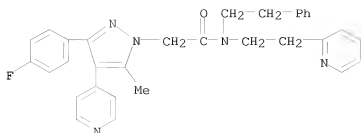
PATENT INFORMATION:

SearchSTN

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6979686	B1	20051227	US 2001-21780	20011207
AU 2003200580	A1	20030501	AU 2003-200580	20030217
US 7071198	B2	20060704	US 2004-840734	20040505
US 20070078146	A1	20070405		
PRIORITY APPLN. INFO.:			US 1997-47570P	P 19970522
			AU 1998-75883	A3 19980522
			US 1998-196623	A2 19981120
			US 2000-513351	A3 20000224
			US 2001-21780	A3 20011207
OTHER SOURCE(S):	MARPAT 144:69823			
GI				



- AB Title compds. [I; R1 = H, OH, NH2, (cyclo)alk(en)yl, acyl, aryl, etc.; R2 = H, halo, mercapto, aryl, heterocyclyl, etc.; R3 = (un)substituted pyridinyl, pyrimidinyl, quinolinyl, etc.; R4 = H, alkyl, (un)substituted Ph, etc.; and pharmaceutically acceptable salts or tautomers thereof] were prepared by solution phase and solid phase parallel array reactions of ketones with hydrazines. Thus, R3CH2COMe (R3 = 4-pyridinyl) was condensed with 3,4-F(MeO)C6H3CHO to give the butenone (80%), which was cyclocondensed with TsNHNH2 to afford the title compound II (20.7%). The latter inhibited human p38 kinase activity in vitro with IC50 of 4.6 μ M and inhibited tumor necrosis factor α (TNF α) and interleukin 1 β (IL-1 β) release from human peripheral blood mononuclear cells following stimulation with lipopolysaccharide with IC50 of 0.5 μ M. Thus, I are useful for the treatment of inflammation, arthritis, asthma, and other disorders mediated by p38 kinase and TNF α . The pharmaceutical compns. comprising the compound I are disclosed.
- IT 216528-02-8P
 RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
 (p38 kinase inhibitor; preparation of heteroarylpyrazole p38 kinase inhibitors by cyclocondensation of hydrazines with ketones)
- RN 216528-02-8 HCAPLUS
- CN 1H-Pyrazole-1-acetamide, 3-(4-fluorophenyl)-5-methyl-N-(2-phenylethyl)-4-(4-pyridinyl)-N-[2-(2-pyridinyl)ethyl]- (CA INDEX NAME)



REFERENCE COUNT: 87 THERE ARE 87 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 6 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:1159842 HCAPLUS

DOCUMENT NUMBER: 143:416509

TITLE: Somatostatin increases voltage-gated K⁺ currents in GH3 cells through activation of multiple somatostatin receptors

AUTHOR(S): Yang, Seung-Kwon; Parkinson, Helena C.; Blake, Allan D.; Keating, Damien J.; Chen, Chen

CORPORATE SOURCE: Prince Henry's Institute of Medical Research, Monash University, Melbourne, 3168, Australia

SOURCE: Endocrinology (2005), 146(11), 4975-4984

CODEN: ENDOAO; ISSN: 0013-7227

PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The secretion of GH by somatotropes is inhibited by somatostatin (SRIF) through five specific membrane receptors (SSTRs). SRIF increases both transient outward (I_A) and delayed rectifying (I_K) K⁺ currents. We aim to clarify the subtype(s) of SSTRs involved in K⁺ current enhancement in GH3 somatotrope cells using specific SSTR subtype agonists. Expression of all five SSTRs was confirmed in GH3 cells by RT-PCR. Nystatin-perforated patch clamp was used to record voltage-gated K⁺ currents. We first established the presence of I_A and I_K type K⁺ currents in GH3 cells using different holding potentials (-40 or -70 mV) and specific blockers (4-aminopyrimidine and tetraethylammonium chloride). SRIF (200 nM) increased the amplitude of both I_A and I_K in a fully reversible manner. Various concns. of each specific SSTR agonist were tested on K⁺ currents to find the maximal effective concentration. Activation of SSTR2 and SSTR4 by their resp. agonists, L-779976 and L-803087 (10 nM), increased K⁺ current amplitude without preference to I_A or I_K, and abolished any further increase by SRIF. Activation of SSTR1 and SSTR5 by their resp. agonists, L-797591 or L-817818 (10 nM), increased K⁺ current amplitude, but SRIF evoked a further increase. The SSTR3 agonist L-796778 (10 nM) did not affect the K⁺ currents or the response to SRIF. These results indicate that SSTR1, -2, -4, and -5 may all be involved in the enhancement of K⁺ currents by SRIF but that only the activation of SSTR2 or -4 results in the full activation of K⁺ current caused by SRIF.

IT 217480-24-5, L-797591

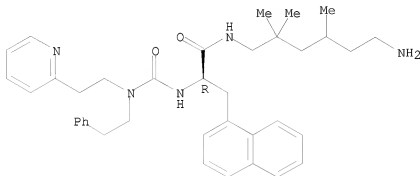
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(somatostatin increases voltage-gated potassium currents in GH3 cells through activation of multiple somatostatin receptors)

RN 217480-24-5 HCAPLUS

SearchSTN

CN 1-Naphthalenepropanamide, N-(6-amino-2,2,4-trimethylhexyl)- α -[[[(2-phenylethyl)[2-(2-pyridinyl)ethyl]amino]carbonyl]amino]-, (α R)- (CA INDEX AMINO)

Absolute stereochemistry.



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 7 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:1133092 HCAPLUS

DOCUMENT NUMBER: 144:44558

TITLE: Steric protection of a photosensitizer in a N,N-bis[2-(2-pyridyl)ethyl]-2-phenylethylamine-copper(II) bowl that enhances red light-induced DNA cleavage activity

AUTHOR(S): Dhar, Shanta; Nethaji, Munirathinam; Chakravarty, Akhil R.

CORPORATE SOURCE: Department of Inorganic & Physical Chemistry, Indian Institute of Science, Bangalore, 560012, India

SOURCE: Inorganic Chemistry (2005), 44(24), 8876-8883
CODEN: INOCAJ; ISSN: 0020-1669

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 144:44558

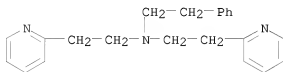
AB Ternary copper(II) complexes [Cu(py2phe)B](ClO4)2 (1-3), where py2phe is the tripodal ligand N,N-bis[2-(2-pyridyl)ethyl]-2-phenylethylamine and B is a heterocyclic base (viz., 1,10-phenanthroline (phen, 1), dipyrido[3,2-d:2',3'-f]quinoxaline (dpq, 2), or dipyrido[3,2-a:2',3'-c]phenazine (dppz, 3)), were prepared and their DNA-binding and photoinduced DNA-cleavage activities were studied. Complex 1 was structurally characterized by single crystal x-ray crystallog. The mol. structure shows an axially elongated square-pyramidal (4 + 1) coordination geometry in which the phen ligand binds at the basal plane. The tripodal ligand py2phe displays an axial-equatorial binding mode with the amine nitrogen bonded at the axial site. A chemical significant CH- π interaction involving the CH moiety of the Ph group of the tripodal ligand and the aromatic ring of phen is observed. The complexes display good binding propensity

to calf thymus DNA giving a relative order of 3 (dppz) > 2 (dpq) > 1 (phen). The DNA binding consts. (Kb) for 1-3, determined from absorption

Updated Search

spectral studies, are 6.2 + 103, 1.0 + 104, and 5.7 + 104 M-1, resp. The complexes show chemical nuclease activity in the presence of 3-mercaptopropionic acid as a reducing agent forming hydroxyl radicals as the cleavage active species. The photoinduced DNA-cleavage activity of the complexes was studied using UV radiation of 365 nm and red light of 632.8 and 694 nm. The phen complex in absence of any photosensitizing moiety does not show any DNA cleavage upon photoirradn. The dpq and dppz ligands with their photoactive quinoxaline and phenazine moieties display significant photoinduced DNA-cleavage activity. The dppz complex is more active than its dpq analog because of the better steric protection of the DNA-bound photosensitizing dppz ligand from the solvent mols. Control expts. reveal the formation of singlet oxygen in the light-induced DNA-cleavage reactions. The observed efficient photoinduced DNA-cleavage activity of 2 and 3 is akin to the light switch effect known for the tris-chelates of ruthenium(II).

IT 31582-30-6, N,N-Bis[2-(2-pyridyl)ethyl]-2-phenylethylamine
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of copper bis(pyridylethyl)phenylethylamine phenanthroline, dipyridoquinoxaline and dipyridophenazine complexes)
 RN 31582-30-6 HCAPLUS
 CN 2-Pyridineethanamine, N-(2-phenylethyl)-N-[2-(2-pyridinyl)ethyl]- (CA INDEX NAME)



REFERENCE COUNT: 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 8 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:540564 HCAPLUS

DOCUMENT NUMBER: 143:77864

TITLE: Urea-based peptidomimetics as somatostatin receptor subtype 1 (SSTR1) modulators, their preparation and use in therapy

INVENTOR(S): Knuuttila, Pia; Salo, Harri; Tomperi, Jussi; Wurster, Siegfried; Hoffren, Anna-Marja

PATENT ASSIGNEE(S): Oy Juvantia Pharma Ltd., Finland

SOURCE: PCT Int. Appl., 58 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

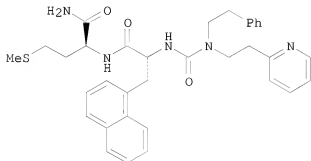
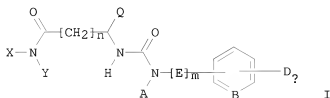
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005056520	A1	20050623	WO 2004-FI750	20041209
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,				

SearchSTN

LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
 NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
 EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
 RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
 MR, NE, SN, TD, TG
 CA 2547863 A1 20050623 CA 2004-2547863 20041209
 EP 1692099 A1 20060823 EP 2004-805145 20041209
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS
 JP 2007513928 T 20070531 JP 2006-543564 20041209
 PRIORITY APPLN. INFO.: FI 2003-1824 A 20031212
 US 2003-509073P P 20031212
 WO 2004-FI750 W 20041209
 OTHER SOURCE(S): CASREACT 143:77864; MARPAT 143:77864
 GI



AB The invention relates to a group of novel urea-based peptidomimetics I, which are modulators of somatostatin receptor subtype 1 (SSTR1). In compds. I, X is H, (un)substituted aryl, (un)substituted heteroaryl, etc.; Y is H, C1-6 alkyl, C3-7 cycloalkyl, or C3-7 cycloalkyl-C1-3 alkyl; Q is aryl, aryl-C1-6 alkyl, heteroaryl, or heteroaryl-C1-6 alkyl, where aryl and heteroaryl are optionally substituted with one to three substituents and alkyl is optionally substituted with cycloalkyl, heterocyclyl, aryl, or heteroaryl; A is (un)substituted C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, (un)substituted cycloalkyl, (un)substituted heterocyclyl,

(un)substituted aryl, or (un)substituted heteroaryl; B is N or C (with D attached); D is independently selected from H, halo, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, amino, NO₂, or cyano; E is (un)substituted C; h is 0-4; n is 0 or 1; and m is 0-3; provided that A is not 2-hydroxyethyl, and with 1 specific exclusion. The invention also relates to the preparation of I, pharmaceutical compns. containing I as an active ingredient with at least one pharmaceutically acceptable carrier, as well as to the use of I for the treatment or prevention of diseases or conditions involving SSTR1. Rink amide resin was washed and coupled with N-Fmoc-L-methionine followed by removal of the Fmoc protecting group, coupling with Fmoc-3-naphthalen-1-yl-D-alanine [i.e., (R)-2-(Fmoc-amino)-3-(naphth-1-yl)-propanoic acid], and deprotection. The resulting amine underwent acylation with 4-nitrophenyl chloroformate followed by substitution with phenethyl(2-pyridin-2-ylethyl)amine (preparation given) and cleavage from the resin to give urea-based peptidomimetic II. The compds. of the invention are selective for SSTR1 and SSTR4 over SSTR2, SSTR3, and SSTR5, and can therefore be useful in combination with a detectable label for tissue imaging, or as carriers for another therapeutically active compound to be targeted to tissues containing SSTR1. Compound II has a K_i value of 19 nM for SSTR1, 640

nM

for SSTR4, and >10,000 nM for SSTR2, SSTR3, and SSTR5. A large set of other compds. of the invention had a K_i value of less than 100 nM for SSTR1.

IT

855308-83-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of urea-based peptidomimetics as somatostatin receptor subtype 1 modulators)

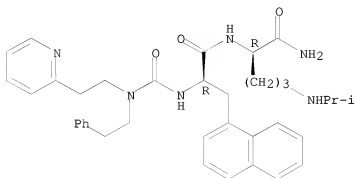
RN

855308-83-7 HCAPLUS

CN

D-Ornithinamide, 3-(1-naphthalenyl)-N-[[2-(2-phenylethyl)[2-(2-pyridinyl)ethyl]amino]carbonyl]-D-alanyl-N5-(1-methylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

3

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 9 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:471946 HCAPLUS

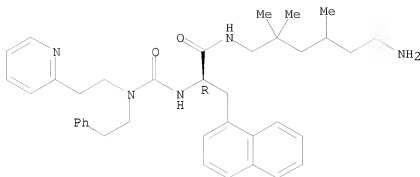
Updated Search

SearchSTN

DOCUMENT NUMBER: 143:1283
 TITLE: Materials and methods using a synergistic combination of an inhibitor of mammalian Target of Rapamycin (mTOR) and an inhibitor of Platelet-Derived Growth Factor Receptor (PDGF-R) for inhibiting neointimal hyperplasia
 INVENTOR(S): Hayry, Pekka Juha
 PATENT ASSIGNEE(S): Oy Helsinki Transplantation R & D Ltd., Finland
 SOURCE: PCT Int. Appl., 102 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005049021	A1	20050602	WO 2004-EP12406	20041103
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
PRIORITY APPLN. INFO.:			US 2003-517165P	P 20031103
OTHER SOURCE(S):	MARPAT 143:1283			
AB	The present invention discloses a combination of an inhibitor of a mammalian Target of Rapamycin (mTOR) and an inhibitor of a Platelet-Derived Growth Factor Receptor (PDGF-R) for treating or preventing neointimal hyperplasia. The effect is synergistic and long-lasting. In some embodiments, the mTOR inhibitor comprises rapamycin and the PDGF-R inhibitor comprises imatinib mesylate. The inhibitors may be administered in a common mixture or as a sep. composition, they may also be administered in any number of different ways including orally, e.g., by pill, or locally, e.g., by means of a stent coating.			
IT	217480-24-5, L-797591 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (mTOR inhibitor-PDGF receptor inhibitor synergistic combination for inhibition of neointimal hyperplasia)			
RN	217480-24-5 HCAPLUS			
CN	1-Naphthalenepropanamide, N-(6-amino-2,2,4-trimethylhexyl)- α -[[[(2-phenylethyl)[2-(2-pyridinyl)ethyl]amino]carbonyl]amino]-, (aR)- (CA INDEX NAME)			

Absolute stereochemistry.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 10 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:1079152 HCAPLUS

DOCUMENT NUMBER: 142:127782

TITLE: Role of somatostatin receptors on gastric acid secretion in wild-type and somatostatin receptor type 2 knockout mice

AUTHOR(S): Piqueras, Laura; Martinez, Vicente

CORPORATE SOURCE: Department of Physiology, Pharmacology and Toxicology, Cardenal Herrera CEU University, Valencia, Spain

SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology (2004), 370(6), 510-520

CODEN: NSAPCC; ISSN: 0028-1298

PUBLISHER: Springer GmbH

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Somatostatin, probably acting through somatostatin type 2 receptors (SSTR2), is the main inhibitor of gastric acid secretion. We characterized gastric acid secretion in SSTR2 knockout mice, and used preferential somatostatin receptor agonists to assess the relative role of SSTR1, 2, 3, 4, and 5 on gastric acid secretion. Basal gastric acid secretion and the secretory response to a meal were similar in conscious wild-type and knockout mice. However, under urethane anesthesia, which releases endogenous somatostatin, SSTR2 knockout mice had a basal secretion 11-15-fold higher than wild-type animals ($\mu\text{mol}/10$ min: 1.40 ± 0.09 vs. 0.10 ± 0.01 , $p < 0.05$). Gastrin immunoneutralization or H2 receptors blockade (cimetidine), but not cholinergic blockade (atropine), reduced the high basal secretion in SSTR2 knockout mice. In SSTR2 knockout mice, gastrin and histamine stimulated acid secretion with similar efficacy, while in wild-type mice histamine was more effective than gastrin. SSTR2 knockout mice showed also a hypersecretory response to pylorus ligation compared with wild-type animals. In wild-type mice, somatostatin-14, SMS 201-995, and the SSTR2-preferential agonist, DC 32-87, inhibited gastrin-stimulated acid secretion with an order of potency $\text{SMS 201-995} > \text{DC 32-87} > \text{somatostatin-14}$. Preferential agonists for the SSTR1, 3, 4, and 5 were devoid of any effect. None of the compounds tested affected the high basal secretion observed under urethane anesthesia in SSTR2 knockout mice. These results show that gastric antisecretory effects of peripheral somatostatin are mediated solely through SSTR2. In the absence of functional SSTR2 other somatostatin receptors do not

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compensate for the lack somatostatin-SSTR2-mediated inhibition. Basal acid secretion and the response to a meal are normal in conscious SSTR2 knockout mice, suggesting the presence of somatostatin-independent mechanisms that compensate for the lack of somatostatin-SSTR2-mediated inhibitory responses.

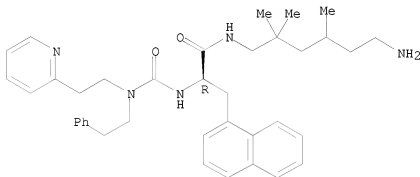
IT 217480-24-5, L-797591

RL: BSU (Biological study, unclassified); BIOL (Biological study) (effects of somatostatin-14 and somatostatin-related compds. on pentagastrin-stimulated gastric acid secretion in wild-type and somatostatin receptor type 2 knockout mice)

RN 217480-24-5 HCAPLUS

CN 1-Naphthalenepropanamide, N-(6-amino-2,2,4-trimethylhexyl)- α -[[[(2-phenylethyl)[2-(2-pyridinyl)ethyl]amino]carbonyl]amino]-, (α R)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 11 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:776233 HCAPLUS

DOCUMENT NUMBER: 141:343783

TITLE: The somatostatin receptor (sst1) modulates the release

of somatostatin in the nucleus accumbens of the rat

AUTHOR(S): Vasilaki, Anna; Papasava, Despina; Hoyer, Daniel;

Thermos, Kyriaki

CORPORATE SOURCE: Faculty of Medicine, Department of Basic Sciences,

Laboratory of Pharmacology, University of Crete,

Heraklion, Crete, 71110, Greece

SOURCE: Neuropharmacology (2004), 47(4), 612-618

CODEN: NEPHBW; ISSN: 0028-3908

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The aim of the present study was to examine the function of the somatostatin receptor (sst1) in the nucleus accumbens (NAc) of the basal ganglia. Radioligand binding studies were performed in rats to assess the presence of the receptor, while in vivo microdialysis studies were performed to examine its role in somatostatin release. CH-275, which is selective for sst1, MK-678, selective for sst2 and L-803,087, selective for sst4 receptors displaced [125I]-Tyr11-somatostatin specific binding in

a concentration-dependent manner with IC₅₀ values of 75, 0.21 and 11 nM, resp. Infusion of CH-275 (10⁻⁵, 10⁻⁶ or 10⁻⁷ M) in the NAC of freely moving rats resulted in a decrease in somatostatin levels only at the concentration of 10⁻⁵ M. This effect was reversed by 10⁻⁵ M of the selective sst1 antagonist SRA-880. The sst1 agonist L-797591 (10⁻⁵ M) mimicked the effect of CH-275, while MK-678 and L-803,087 at the same concentration were unable to influence somatostatin levels. These results provide functional evidence to demonstrate that the sst1 receptor modulates somatostatin release in the basal ganglia.

IT 217480-24-5, L-797591

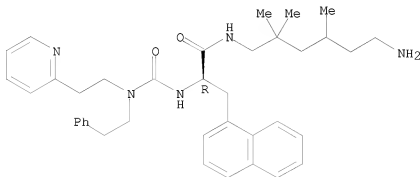
RL: PAC (Pharmacological activity); BIOL (Biological study)

(nucleus accumbens somatostatin receptor sst1 inhibitory modulation of somatostatin release in rats)

RN 217480-24-5 HCAPLUS

CN 1-Naphthalenepropanamide, N-(6-amino-2,2,4-trimethylhexyl)- α -[[[(2-phenylethyl)[2-(2-pyridinyl)ethyl]amino]carbonylamino]-, (α R)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 12 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:683275 HCAPLUS

DOCUMENT NUMBER: 141:311749

TITLE: Expression of somatostatin receptors in normal and cirrhotic human liver and in hepatocellular carcinoma
 AUTHOR(S): Reynaert, H.; Rombouts, K.; Vandermonde, A.; Urbain, D.; Kumar, U.; Bioulac-Sage, P.; Pinzani, M.; Rosenbaum, J.; Geerts, A.

CORPORATE SOURCE: Brussels, Belg.

SOURCE: Gut (2004), 53(8), 1180-1189

CODEN: GUTAK; ISSN: 0017-5749

PUBLISHER: BMJ Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Background: Somatostatin analogs have been used with conflicting results to treat advanced hepatocellular carcinoma (HCC). The aim of this study was to investigate expression of somatostatin receptor (SSTR) subtypes in human liver, and to examine the effect of selective SSTR agonists on proliferation, apoptosis, and migration of hepatoma cells (HepG2, HuH7)

and hepatic stellate cells (HSCs). Methods: Expression of SSTRs in cell lines, normal and cirrhotic liver, and HCC was examined by immunohistochem. and reverse transcription-polymerase chain reaction. Effects of SSTR agonists on proliferation and apoptosis of tumor cells and HSCs were assessed by the 5-bromo-2' deoxyuridine and TUNEL methods, resp. The influence of SSTR agonists on migration was investigated using Boyden chambers. Results: In normal liver, both hepatocytes and HSCs were neg. for all five SSTRs. Cirrhotic liver and HCC as well as cultured hepatoma cells and HSCs expressed all five SSTRs, both at the protein and mRNA levels, except for HuH7 cells which did not immunoreact with SSTR3. None of the agonists influenced proliferation or apoptosis. However, compared with untreated cells, L-797,591, an SSTR1 agonist, reduced migration of HepG2, HuH7, and HSCs significantly to 88 (7)% (p<0.05), 83 (11)% (p<0.05), and 67 (13)% (p<0.01), resp. Conclusions: Cirrhotic liver and HCC express SSTRs. Although the somatostatin analogs used in this study did not affect proliferation and apoptosis, stimulation of SSTR1 may decrease invasiveness of HCC by reducing migration of hepatoma cells and/or HSCs. Clin. trials evaluating somatostatin analogs for the treatment of HCC should take these findings into account.

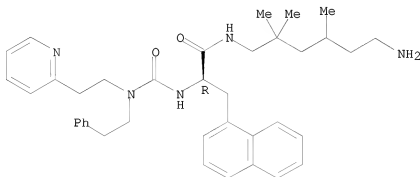
IT 217480-24-5, L-797591

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(expression of somatostatin receptors in normal and cirrhotic human liver and in hepatocellular carcinoma)

RN 217480-24-5 HCAPLUS

CN 1-Naphthalenepropanamide, N-(6-amino-2,2,4-trimethylhexyl)- α -[[[(2-phenylethyl)[2-(2-pyridinyl)ethyl]amino]carbonyl]amino]-, (α R)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 13 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:267292 HCAPLUS

DOCUMENT NUMBER: 140:287259

TITLE: Preparation of amide and sulfonamide ligands for the estrogen receptor

INVENTOR(S): O'Keefe Cameron, Kimberly; Chesworth, Richard

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

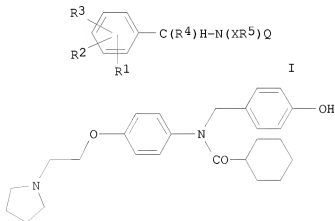
SOURCE: PCT Int. Appl., 143 pp.

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DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

CODEN: PIXXD2
 Patent
 English

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026823	A1	20040401	WO 2003-IB3824	20030908
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2499490	A1	20040401	CA 2003-2499490	20030908
AU 2003263402	A1	20040408	AU 2003-263402	20030908
EP 1542967	A1	20050622	EP 2003-797427	20030908
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
BR 2003014126	A	20050628	BR 2003-14126	20030908
JP 2006508061	T	20060309	JP 2004-537389	20030908
US 20040110767	A1	20040610	US 2003-666811	20030917
US 7053212	B2	20060530		
MX 2005PA03054	A	20050527	MX 2005-PA3054	20050318
PRIORITY APPLN. INFO.:			US 2002-412338P	P 20020920
			WO 2003-IB3824	W 20030908
OTHER SOURCE(S):		MARPAT 140:287259		
GI				



AB The present invention provides amides and sulfonamides (shown as I; variables defined below; many of the examples contain the pyrrolidine

ring, e.g. II) that are estrogen receptor (ER) ligands (no data), the pharmaceutically acceptable salts, stereoisomers, and prodrugs thereof, and the pharmaceutically acceptable salts of the prodrugs. The invention further provides pharmaceutical compns. comprising I, and methods for treating or preventing diseases, disorders, conditions, or symptoms mediated by an ER (e.g. female sexual dysfunction, postmenopausal syndrome, osteoporosis, elevated serum cholesterol levels, and breast or uterine cancer) which comprise administering to a mammalian subject in need of treatment therewith, an effective amount of I, or a pharmaceutically acceptable salt, stereoisomer, or prodrug thereof, or a pharmaceutically acceptable salt of the prodrug, or a pharmaceutical composition comprising I, or a pharmaceutically acceptable salt, stereoisomer, or prodrug thereof, or a pharmaceutically acceptable salt of the prodrug. The invention further provides pharmaceutical compns. comprising combinations of I and ≥ 1 of NaF, estrogen, a bone anabolic agent, a growth hormone or growth hormone secretagogue, a prostaglandin agonist/antagonist, and a parathyroid hormone, and methods of treating or preventing diseases, disorders, conditions, or symptoms mediated by an ER comprising the administration of an effective amount of such combination to a mammalian subject in need of treatment therewith. Although the methods of preparation are not claimed, 212 example preps. are included. For example, II was prepared in 41% yield by base hydrolysis of its p-toluenesulfonic acid ester, which in turn was prepared N-acylation of toluene-4-sulfonic acid 4-[[[4-[2-(pyrrolidin-1-yl)ethoxy]phenyl]amino]methyl]phenyl ester by cyclohexanecarbonyl chloride. Toluene-4-sulfonic acid 4-[[[4-[2-(pyrrolidin-1-yl)ethoxy]phenyl]amino]methyl]phenyl ester was prepared in 2 steps (71 and 80%, resp., yields) starting with tosylate formation from 4-hydroxybenzaldehyde followed by imine formation with [4-[2-(pyrrolidin-1-yl)ethoxy]phenyl]amine and reduction by NaBH₄. For I: Q = R⁹- and Z-substituted Ph or six-membered heteroaryl ring containing 1-2 N atoms; R¹, R², R³, and R⁹ are H, hydroxy, halogen, cyano, -(C1-C6) alkyl (un)substituted with 1-3 F atoms and -(C1-C6) alkyl (un)substituted with 1-3 F atoms. R⁴ is H or -(C1-C6) alkyl; R⁵ is -(C1-C7) alkyl (un)substituted with 1-6 halogen atoms, -(C2-C6) alkenyl, -(C2-C6) alkenyl-M, or -(CH₂)_n-M, wherein n = 0-5 and M is (i) a fully saturated 3-8 membered ring, or a partially saturated, or fully saturated 5-8 membered ring optionally having = 1-4 heteroatoms independently O, N, and S, or (ii) a bicyclic ring comprising two fused partially saturated, fully saturated, or fully unsatd. 5- or 6-membered rings optionally having 1-4 heteroatoms independently O, N and S. X is CO or SO₂; Z is -O(CH₂)_n-NR^aR^b, -(CH₂)_n-NR^aR^b, -CH₂-CH-C(O)-NR^aR^b, -(CH₂)_n-COOH, -CH₂-CH-COOH, -O(C1-C6) alkyl, -CH₂-CH-CO₂(C1-C6) alkyl, or -(CH₂)_n-OH; addnl. details are given in the claims.

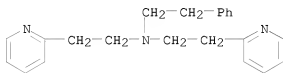
IT 675868-06-1P, N-(2-Chloro-4-hydroxybenzyl)-2,4,6-trimethyl-N-[4-[3-[methyl[2-(pyridin-2-yl)ethyl]amino]propyl]phenyl]benzenesulfonamide RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of amide and sulfonamide ligands for estrogen receptor)

RN 675868-06-1 HCAPLUS

CN Benzenesulfonamide, N-[(2-chloro-4-hydroxyphenyl)methyl]-2,4,6-trimethyl-N-[4-[3-[methyl[2-(2-pyridinyl)ethyl]amino]propyl]phenyl]- (CA INDEX NAME)

orbital of the Ph ring. The Cu(I) complexes 1x reacted with O₂ at -80° in CH₂Cl₂ to give the corresponding (μ - η^2 : η^2 -peroxo)dicopper(II) complexes 4, the formation rates kobs of which were significantly retarded by stronger d- π interaction, while complexes 2 and 3, which exhibit the strongest d- π interaction showed significantly lower reactivity toward O₂ under the same exptl. conditions. Thus, the d- π interaction was demonstrated for the 1st time to affect the Cu(I)-dioxygen reactivity, and represents a new aspect of ligand effects in Cu(I)-dioxygen chemical

IT 31582-30-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and reaction of tridentate bis(pyridylethyl)amine ligands with copper complex and control of copper(I)-dioxygen reactivity)
 RN 31582-30-6 HCAPLUS
 CN 2-Pyridineethanamine, N-(2-phenylethyl)-N-[2-(2-pyridinyl)ethyl]- (CA INDEX NAME)



REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 15 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:465211 HCAPLUS

DOCUMENT NUMBER: 139:160151

TITLE: Pharmacological characterization of native somatostatin receptors in AtT-20 mouse tumor corticotrophs

AUTHOR(S): Cervia, Davide; Nunn, Caroline; Fehlmann, Dominique; Langenegger, Daniel; Schuepbach, Edi; Hoyer, Daniel

CORPORATE SOURCE: Dipartimento di Fisiologia e Biochimica "G. Moruzzi", Università di Pisa, Pisa, 56127, Italy

SOURCE: British Journal of Pharmacology (2003), 139(1), 109-121

CODEN: BJPCBM; ISSN: 0007-1188

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The mouse corticotroph tumor cell line AtT-20 is a useful model to investigate the physiol. role of native somatostatin (SRIF, Somatotropin release inhibitory factor) receptor subtypes (sst1 - sst5). The objective of this study was to characterize the pharmacol. features and the functional effects of SRIF receptors expressed by AtT-20 cells using radioligand binding and cAMP accumulation. [125I]LTT-SRIF-28, [125I]CGP 23996, [125I]Tyr10-cortistatin-14 and [125I]Tyr3-octreotide labeled SRIF receptor binding sites with high affinity and in a saturable manner (Bmax = 315, 274, 239 and 206 fmol mg⁻¹, resp.). [125I]LTT-SRIF-28 labels significantly more sites than [125I]Tyr10 - cortistatin-14 and [125I]Tyr3 - octreotide as seen previously in cells expressing pure populations of

sst2 or sst5 receptors. SRIF analogs displaced the binding of the four radioligands. Sst2/5 receptor-selective ligands showed much higher affinity than sst1/3/4 receptor-selective ligands. The binding profile of [125I]Tyr3-octreotide was different from that of [125I]LTT-SRIF-28, [125I]CGP 23996 and [125I]Tyr10-cortistatin-14. The sst5/1 receptor-selective ligand L-817,818 identified two binding sites, one with subnanomolar affinity (sst5 receptors) and one with micromolar affinity (sst2 receptors); however, the proportions were different: 70-80% high affinity with [125I]LTT-SRIF-28, [125I]CGP 23996, [125I]Tyr10-cortistatin-14, but only 20% with [125I]Tyr3-octreotide. SRIF analogs inhibited the forskolin-stimulated cAMP levels depending on concentration sst2/5 receptor-selective ligands were highly potent, whereas sst1/3/4 receptor-selective ligands had no significant effects. The sst2 receptor antagonist D-Tyr8-CYN 154806 competitively antagonized the effects of SRIF-14 and sst2 receptor-preferring agonists, but not those of L-817,818. The complex binding properties of SRIF receptor analogs indicate that sst2 and sst5 receptors are the predominant SRIF receptors expressed on Att-20 cell membranes with no or only negligible presence of sst1, sst3 and sst4 receptors. In the functional studies using cAMP accumulation, only sst2 and sst5 receptors appear to play a role. However, the "predominant" receptor appears to be the sst2 receptor, although sst5 receptors can also mediate the effect, when the ligand is not able to activate sst2 receptors. This clearly adds flexibility to SRIF-mediated functional effects and suggests that the physiol. role of SRIF and its analogs may be mediated preferentially via one subtype over another.

IT 217480-24-5, L-797591

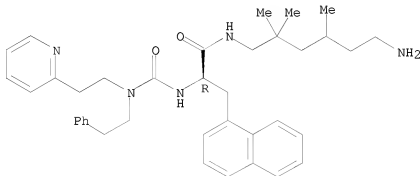
RL: PAC (Pharmacological activity); BIOL (Biological study)

(pharmacol. characterization of native somatostatin receptors and their ligands in Att-20 mouse tumor corticotrophs)

RN 217480-24-5 HCAPLUS

CN 1-Naphthalenepropanamide, N-(6-amino-2,2,4-trimethylhexyl)- α -[[[(2-phenylethyl)[2-(2-pyridinyl)ethyl]amino]carbonyl]amino]-, (α R)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 16 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:438472 HCAPLUS

DOCUMENT NUMBER: 139:162199

SearchSTN

TITLE: Identification of somatostatin receptors controlling growth hormone and thyrotropin secretion in the chicken using receptor subtype-specific agonists

AUTHOR(S): Geris, K. L.; De Groef, B.; Rohrer, S. P.; Geelissen, S.; Kuhn, E. R.; Darras, V. M.

CORPORATE SOURCE: Laboratory of Comparative Endocrinology, Katholieke Universiteit Leuven, Louvain, B-3000, Belg.

SOURCE: Journal of Endocrinology (2003), 177(2), 279-286
CODEN: JOENAK; ISSN: 0022-0795

PUBLISHER: Society for Endocrinology

DOCUMENT TYPE: Journal

LANGUAGE: English

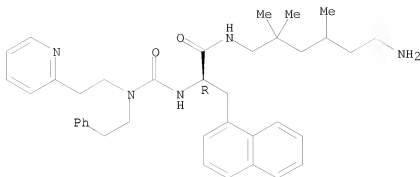
AB Somatostatin (SRIH) functions as an endocrine mediator in processes such as growth, immune resistance and reproduction. Five SRIH receptors (sstr1-5) have been identified in mammals, where they are expressed in both the brain and peripheral tissues. To study the specific function of each receptor subtype, specific agonists (ag1-5) have been synthesized. The high degree of homol. between mammalian and avian SRIH receptors suggests that these agonists might also be used in chickens. In this paper the authors describe two in vitro protocols (static incubation and perfusion system) to identify the SRIH receptors controlling the secretion of GH and TSH from the chicken pituitary. The authors found that basal GH or TSH secretion were never affected when SRIH or an agonist (1 μ M) were added. SRIH diminished the GH as well as the TSH response to TSH-releasing hormone (TRH; 100 nM) in both systems. The authors' results have indicated that the SRIH actions at the level of the pituitary are regulated through specific receptor subtypes. In both the static and flow incubations, ag2 lowered the GH response to TRH, whereas stimulated TSH release was diminished by both ag2 and ag5. Ag3 and ag4 tended to increase rather than decrease the responsiveness of both pituitary cell types to TRH in perfusion studies. The authors' data have indicated that SRIH inhibits chicken pituitary function throughsstr2 andsstr5. Onlysstr2 seems to be involved in the control of chicken GH release, whereas bothsstr2 andsstr5 inhibit induced GH secretion in mammals. The possible stimulatory action of ag3 and ag4 may point towards a species-specific function ofsstr3 andsstr4.

IT 217480-24-5, L-797591
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(identification of somatostatin receptors controlling growth hormone and TSH secretion in the chicken using receptor subtype-specific agonists)

RN 217480-24-5 HCAPLUS

CN 1-Naphthalenepropanamide, N-(6-amino-2,2,4-trimethylhexyl)- α -[[[(2-phenylethyl)[2-(2-pyridinyl)ethyl]amino]carbonyl]amino]-, (α R)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 17 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:356419 HCAPLUS

DOCUMENT NUMBER: 138:368770

TITLE: Preparation of pyridinylethylamines and amides as anticancer drugs.

INVENTOR(S): Menon, Sanjay R.; Lu, Yingchun; Sakamuri, Sukumar; Chen, Quin-Zene; Khazak, Vladimir; Agarwal, Seema

PATENT ASSIGNEE(S): Morphochem Aktiengesellschaft fuer Kombinatorische Chemie, Germany

SOURCE: PCT Int. Appl., 66 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003037865	A1	20030508	WO 2002-EP12222	20021031
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2468761	A1	20030508	CA 2002-2468761	20021031
AU 2002351814	A1	20030512	AU 2002-351814	20021031
EP 1442018	A1	20040804	EP 2002-787539	20021031
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 20050228017	A1	20051013	US 2005-497449	20050330
PRIORITY APPLN. INFO.:			US 2001-335300P	P 20011031
			WO 2002-EP12222	W 20021031

OTHER SOURCE(S): MARPAT 138:368770

AB (R3Y)(R1X)NUR2 [n = 0-5; X, Y = CH2, CO, SO2, CONH; R1 = (substituted)]

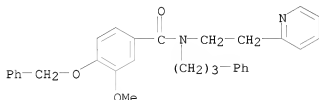
aryl, aralkyl, heteroaryl, heteroarylalkyl; R2 = (substituted) heteroalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, heterocycloalkyl, heteroalkylcycloalkyl; R3 = (substituted) alkyl, alkenyl, alkynyl, heteroalkyl, cycloalkyl, alkylcycloalkyl, heterocycloalkyl, heteroalkylcycloalkyl, aryl, heteroaryl, heteroarylalkyl, aralkyl], were prepared. Thus, N-(4-benzyloxy-3-methoxybenzyl)-N-(2-pyridin-2-ylethyl)amine (preparation given) in C1CH2CH2Cl was treated with polymer-supported morpholine and 2-chlorobenzoyl chloride followed by stirring for 24 h. Polymer-supported isocyanate, polymer-supported tris(2-aminoethyl)amine, and C1CH2CH2Cl were added followed by stirring for 24 h to give 84% N-(4-benzyloxy-3-methoxybenzyl)-N-(2-pyridin-2-ylethyl)-2-chlorobenzamide. Title compds. showed IC50's of 5-60 μ M in secondary luciferase assays in NIH3T3, CHO, or HEK293 cells.

IT 521312-41-4

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of pyridinylethylamines and amides as anticancer drugs)

RN 521312-41-4 HCAPLUS

CN Benzamide, 3-methoxy-4-(phenylmethoxy)-N-(3-phenylpropyl)-N-[2-(2-pyridinyl)ethyl]- (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 18 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:251423 HCAPLUS

DOCUMENT NUMBER: 139:63609

TITLE: Biological activity of somatostatin receptors in GC rat tumor somatotrophs: evidence with sst1-sst5 receptor-selective nonpeptidyl agonists

AUTHOR(S): Cervia, D.; Zizzari, P.; Pavan, B.; Schuepbach, E.; Langenegger, D.; Hoyer, D.; Biondi, C.; Epelbaum, J.; Bagnoli, P.

CORPORATE SOURCE: Dipartimento di Fisiologia e Biochimica "G. Moruzzi", Università di Pisa, Pisa, 56127, Italy

SOURCE: Neuropharmacology (2003), 44(5), 672-685

CODEN: NEPHBW; ISSN: 0028-3908

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

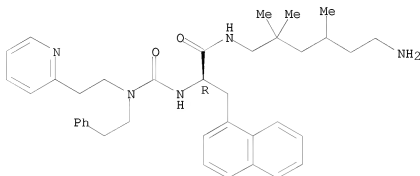
LANGUAGE: English

AB The physiol. actions of somatostatin-14 (SRIF: somatotrophin release inhibitory factor) receptor subtypes (sst1-sst5), which are endogenously expressed in growth cells (GC cells), have not yet been elucidated, although there is evidence that sst2 receptors are neg. coupled to cytosolic free Ca²⁺ concentration ([Ca²⁺]_i) and cAMP accumulation. In addition,

both sst1 and sst2 receptors are neg. coupled to growth hormone (GH) secretion in GC cells. Here the authors report on studies concerning the expression, the pharmacol. and the functional role of native SRIF receptors in GC cells with the use of five nonpeptidyl agonists, highly selective for each of the SRIF receptors. Radioligand binding studies show that sst2 and sst5 receptors are present at different relative densities, while the presence of sst3 and sst4 receptors appears to be negligible. The absence of sst1 receptor binding was unexpected in view of sst1 receptor functional effects on GH secretion. This suggests very efficient receptor-effector coupling of a low-d. population of sst1 receptors. Functionally, only sst2 receptors are coupled to the inhibition of $[Ca^{2+}]_i$ and cAMP accumulation and the selective activation of sst5 receptors facilitates the stimulation of adenylyl cyclase activity through Gi/o proteins. This effect was not observed when sst2 and sst5 receptors were simultaneously activated, suggesting that there is a functional interaction between sst2 and sst5 receptors. In addition, sst1, sst2 and sst5 receptor activation inhibits GH release, further indicating that SRIF can modulate GH secretion in GC cells through mechanisms both dependent and independent on $[Ca^{2+}]_i$ and cAMP-dependent pathways. The present data suggest SRIF-mediated functional effects in GC cells to be very diverse and provides compelling arguments to propose that multiple native SRIF receptors expressed in the same cells are not simply redundant, but contribute to marked signaling diversity.

IT 217480-24-5, L797591
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (biol. activity of somatostatin receptors in GC rat tumor somatotrophs using sst1-sst5 receptor-selective nonpeptidyl agonists)
 RN 217480-24-5 HCAPLUS
 CN 1-Naphthalenepropanamide, N-(6-amino-2,2,4-trimethylhexyl)- α -[[[(2-phenylethyl)[2-(2-pyridinyl)ethyl]amino]carbonyl]amino]-, (α R)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 19 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2003:150531 HCAPLUS
 DOCUMENT NUMBER: 138:187765
 TITLE: Preparation of heteroarylpyrazoles as p38 kinase inhibitors

SearchSTN

INVENTOR(S): Anantanarayan, Ashok; Clare, Michael; Collins, Paul W.; Crich, Joyce Zuowu; Devraj, Rajesh; Flynn, Daniel L.; Geng, Lifeng; Graneto, Matthew J.; Hanau, Cathleen E.; Hanson, Gunnar J.; Hartmann, Susan J.; Hepperle, Michael; Huang, He; Koszyk, Francis J.; Liao, Shuyuan; Metz, Suzanne; Partis, Richard A.; Perry, Thao D.; Rao, Shashidhar N.; Selness, Shaun Raj; South, Michael S.; Stealey, Michael A.; Talley, John Jeffrey; Vazquez, Michael L.; Weier, Richard M.; Xu, Xiangdong; Khanna, Ish K.; Yu, Yi

PATENT ASSIGNEE(S): G.D. Searle and Co., USA

SOURCE: U.S., 415 pp., Cont.-in-part of U.S. Ser. No. 196,623. CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

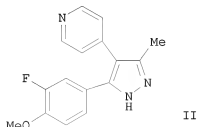
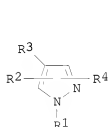
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6525059	B1	20030225	US 2000-513351	20000224
US 6514977	B1	20030204	US 1998-196623	19981120
WO 2000031063	A1	20000602	WO 1999-US26007	19991117
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 2003200580	A1	20030501	AU 2003-200580	20030217
US 7071198	B2	20060704	US 2004-840734	20040505
US 20070078146	A1	20070405		

PRIORITY APPLN. INFO.:

US 1998-196623	A2 19981120
WO 1999-US26007	A1 19991117
US 1997-47570P	P 19970522
AU 1998-75883	A3 19980522
US 1998-83670	A2 19980522
US 2000-513351	A3 20000224
US 2001-21780	A3 20011207

OTHER SOURCE(S): MARPAT 138:187765

GI

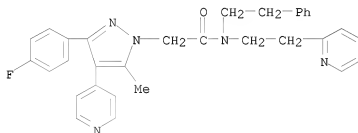


AB Title compds. [I; R1 = H, OH, NH2, (cyclo)alk(en)yl, acyl, aryl, etc.; R2 = (un)substituted piperidinyl; R3 = (un)substituted pyrimidinyl; R4 = (un)substituted Ph; and pharmaceutically acceptable salts or tautomers thereof] were prepared by solution phase and solid phase parallel array reactions of ketones with hydrazines. Thus, R3CH2COMe (R3 = 4-pyridinyl) was condensed with 3,4-F(MeO)C6H3CHO to give the butenone (80%), which was cyclocondensed with TsNHNH2 to afford the title compound II (20.7%). The latter inhibited human p38 kinase activity in vitro with IC50 of 4.6 μ M and inhibited tumor necrosis factor α (TNF α) and interleukin 1 β (IL-1 β) release from human peripheral blood mononuclear cells following stimulation with lipopolysaccharide with IC50 of 0.5 μ M. Thus, I are useful for the treatment of inflammation, arthritis, asthma, and other disorders mediated by p38 kinase and TNF α .

IT 216528-02-8P
 RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
 (p38 kinase inhibitor; preparation of heteroarylpyrazole p38 kinase inhibitors by cyclocondensation of hydrazines with ketones)

RN 216528-02-8 HCAPLUS

CN 1H-Pyrazole-1-acetamide, 3-(4-fluorophenyl)-5-methyl-N-(2-phenylethyl)-4-(4-pyridinyl)-N-[2-(2-pyridinyl)ethyl]- (CA INDEX NAME)



REFERENCE COUNT: 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 20 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:92403 HCAPLUS

DOCUMENT NUMBER: 138:137307

TITLE: Preparation of heteroarylpyrazoles as p38 kinase inhibitors

INVENTOR(S): Anantanarayan, Ashok; Clare, Michael; Collins, Paul W.; Crich, Joyce Zuowu; Devraj, Rajesh; Flynn, Daniel L.; Geng, Lifeng; Graneto, Matthew J.; Hanau, Cathleen E.; Hanson, Gunnar J.; Hartmann, Susan J.; Hepperle, Michael; Huang, He; Koszyk, Francis J.; Liao, Shuyuan; Metz, Suzanne; Partis, Richard A.; Perry, Thao D.; Rao, Shashidhar N.; Selness, Shaun Raj; South, Michael S.; Stealey, Michael A.; Talley, John Jeffrey; Vazquez, Michael L.; Weier, Richard M.; Xu, Xiangdong; Khanna, Ish K.; Yu, Yi

PATENT ASSIGNEE(S): G.D. Searle and Co., USA

SOURCE: U.S., 541 pp., Cont.-in-part of U.S. Ser. No. 83,670.

SearchSTN

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 5
 PATENT INFORMATION:

CODEN: USXXAM

Patent

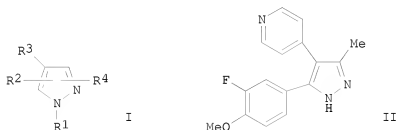
English

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6514977	B1	20030204	US 1998-196623	19981120
CA 2351725	A1	20000602	CA 1999-2351725	19991117
WO 2000031063	A1	20000602	WO 1999-US26007	19991117
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1144403	A1	20011017	EP 1999-965756	19991117
EP 1144403	B1	20041006		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200102001	T2	20011221	TR 2001-2001	19991117
BR 9915420	A	20020122	BR 1999-15420	19991117
HU 2002000130	A2	20020629	HU 2002-130	19991117
EE 200100268	A	20021216	EE 2001-268	19991117
NZ 512344	A	20031128	NZ 1999-512344	19991117
AU 774262	B2	20040624	AU 2000-21454	19991117
AT 278685	T	20041015	AT 1999-965756	19991117
EP 1500657	A1	20050126	EP 2004-23186	19991117
EP 1500657	B1	20070919		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
PT 1144403	T	20050131	PT 1999-965756	19991117
ES 2229809	T3	20050416	ES 1999-965756	19991117
AT 373649	T	20071015	AT 2004-23186	19991117
ES 2289411	T3	20080201	ES 2004-23186	19991117
US 6525059	B1	20030225	US 2000-513351	20000224
ZA 2001003882	A	20021014	ZA 2001-3882	20010514
MX 2001PA05043	A	20010710	MX 2001-PA05043	20010518
NO 2001002456	A	20010719	NO 2001-2456	20010518
BG 105620	A	20020131	BG 2001-105620	20010619
US 6423713	B1	20020723	US 2001-918481	20010731
HK 1040705	A1	20050304	HK 2002-102213	20020322
US 6617324	B1	20030909	US 2002-114297	20020402
AU 2003200580	A1	20030501	AU 2003-200580	20030217
US 20040176433	A1	20040909	US 2003-374781	20030225
US 7153959	B2	20061226		
US 7071198	B2	20060704	US 2004-840734	20040505
US 20070078146	A1	20070405		
PRIORITY APPLN. INFO.:			US 1997-47570P	P 19970522
			US 1998-83670	A2 19980522
			AU 1998-75883	A3 19980522
			US 1998-196623	A 19981120
			EP 1999-965756	A3 19991117

WO 1999-US26007	W 19991117
US 2000-513351	A3 20000224
US 2001-918481	A3 20010731
US 2001-21780	A3 20011207
US 2002-114297	A3 20020402

OTHER SOURCE(S): MARPAT 138:137307

GI



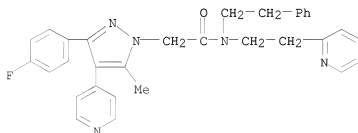
AB Title compds. [I; R¹ = H, OH, NH₂, (cyclo)alk(en)yl, acyl, aryl, etc.; R² = (un)substituted piperidinyl or piperazinyl; R³ = (un)substituted pyrimidinyl; R⁴ = (un)substituted Ph; and pharmaceutically acceptable salts or tautomers thereof] were prepared by solution phase and solid phase parallel array reactions of ketones with hydrazines. Thus, R³CH₂COMe (R³ = 4-pyridinyl) was condensed with 3,4-F(MeO)C₆H₃CHO to give the butenone (80%), which was cyclocondensed with TsNHNH₂ to afford the title compound II (20.7%). The latter inhibited human p38 kinase activity in vitro with IC₅₀ of 4.6 μM and inhibited tumor necrosis factor α (TNFα) and interleukin 1β (IL-1β) release from human peripheral blood mononuclear cells following stimulation with lipopolysaccharide with IC₅₀ of 0.5 μM. Thus, I are useful for the treatment of inflammation, arthritis, asthma, and other disorders mediated by p38 kinase and TNFα.

IT 216528-02-8P

RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(p38 kinase inhibitor; preparation of heteroarylpyrazole p38 kinase inhibitors by cyclocondensation of hydrazines with ketones)

RN 216528-02-8 HCAPLUS

CN 1H-Pyrazole-1-acetamide, 3-(4-fluorophenyl)-5-methyl-N-(2-phenylethyl)-4-(4-pyridinyl)-N-[2-(2-pyridinyl)ethyl]- (CA INDEX NAME)



SearchSTN

REFERENCE COUNT: 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 21 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:528600 HCAPLUS

DOCUMENT NUMBER: 137:257820

TITLE: Somatostatin Receptor Subtypes 2 and 5 Inhibit Corticotropin-Releasing Hormone-Stimulated Adrenocorticotropin Secretion from AtT-20 Cells
 AUTHOR(S): Strowski, Mathias Z.; Dashkevicz, Michael P.; Parmar, Rupa M.; Wilkinson, Hilary; Kohler, Martin; Schaeffer, James M.; Blake, Allan D.

CORPORATE SOURCE: Merck Research Laboratories, Rahway, NJ, USA

SOURCE: Neuroendocrinology (2002), 75(6), 339-346

CODEN: NUNDAJ; ISSN: 0028-3835

PUBLISHER: S. Karger AG

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Somatostatin (SRIH) regulates pituitary ACTH secretion by interacting with a family of homologous G protein-coupled membrane receptors. The SRIH receptor subtypes (sst1-sst5) that control ACTH release remain unknown. Using novel, subtype-selective SRIH analogs, the authors have identified the SRIH receptor subtypes involved in regulating ACTH release from AtT-20 cells, a model for cell line pituitary corticotrophs. Radioligand-binding studies with 125I-SRIH-14 and 125I-SRIH-28 showed that SRIH-14 and SRIH-28 recognized specific, high-affinity and saturable membrane-binding sites. Nonpeptidyl agonists with selectivity for the sst2 (L-779,976; compound 2) or sst1/sst5 (L-817,818; compound 5) receptor subtypes potentially displaced 125I-SRIH-28 from AtT-20 cell membranes, while agonists selective for the sst1 (L-779,591; compound 1), sst3 (L-796,778; compound 3) or sst4 (L-803,087; compound 4) subtypes were inactive. Tyr11-SRIH-14, compound 2 (sst2) or compound 5 (sst5) inhibited forskolin and CRH-induced increases in intracellular cAMP. Furthermore, the sst2 and sst5 agonists potentially inhibited CRH-induced ACTH release from AtT-20 cells. These results provide the first evidence that sst2 and sst5 receptor subtypes, but not sst1, sst3 or sst4, inhibit cAMP accumulation and regulate ACTH secretion in the AtT-20 cell model of the rodent corticotroph.

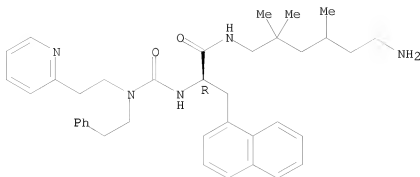
IT 217480-24-5, L-797591

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (SSTR2 and SSTR5 receptor subtypes inhibit CRH-stimulated ACTH secretion from AtT-20 cells)

RN 217480-24-5 HCAPLUS

CN 1-Naphthalenepropanamide, N-(6-amino-2,2,4-trimethylhexyl)- α -[[[(2-phenylethyl)[2-(2-pyridinyl)ethyl]amino]carbonyl]amino]-, (aR)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 22 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:505888 HCAPLUS

DOCUMENT NUMBER: 138:49353

TITLE: The pharmacokinetics of a thiazole benzenesulfonamide β 3-adrenergic receptor agonist and its analogs in rats, dogs, and monkeys: improving oral bioavailability

AUTHOR(S): Stearns, Ralph A.; Miller, Randy R.; Tang, Wei; Kwei, Gloria Y.; Tang, Frank S.; Mathvink, Robert J.; Naylor, Elizabeth M.; Chitty, Dawn; Colandrea, Vincent J.; Weber, Ann E.; Colletti, Adria E.; Strauss, John R.; Keohane, Carol Ann; Feeney, William P.; Iliff, Susan A.; Chiu, Shuet-Hing Lee

CORPORATE SOURCE: Department of Drug Metabolism, Merck Research Laboratories, Rahway, NJ, USA

SOURCE: Drug Metabolism and Disposition (2002), 30(7), 771-777 CODEN: DMDSAI; ISSN: 0090-9556

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The pharmacokinetics and oral bioavailability of (R)-N-[4-[2-[2-[2-hydroxy-2-(pyridin-3-yl)ethyl]amino]ethyl]phenyl]-4-[4-(trifluoromethylphenyl)]thiazol-2-yl]benzenesulfonamide (1), a 3-pyridyl thiazole benzenesulfonamide β 3-adrenergic receptor agonist, were investigated in rats, dogs, and monkeys. Systemic clearance was higher in rats (.apprx.30 mL/min/kg) than in dogs and monkeys (both .apprx.10 mL/min/kg), and oral bioavailability was 17, 27, and 4%, resp. Since systemic clearance was 25 to 40% of hepatic blood flow in these species, hepatic extraction was expected to be low, and it was likely that oral bioavailability was limited either by absorption or a large first-pass effect in the gut. The absorption and excretion of 3H-labeled 1 were investigated in rats, and only 28% of the administered radioactivity was orally absorbed. Subsequently, the hepatic extraction of 1 was evaluated in rats (30%) and monkeys (47%). The low oral bioavailability in rats could be explained completely by poor oral absorption and hepatic first-pass metabolism; in monkeys, oral absorption was either less than in rats or first-pass extraction in the gut was greater. In an attempt to increase oral exposure, the pharmacokinetics and oral bioavailability of two potential

prodrugs of 1, an N-Et [(R)-N-[4-[2-[ethyl[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[4-(4-(trifluoromethyl)phenyl)thiazol-1-2-yl]benzenesulfonamide; 2] and a morpholine derivative [(R)-N-[4-[2-[2-(3-pyridinyl)morpholin-4-yl]ethyl]phenyl]-4-[4-(4-(trifluoromethyl)phenyl)thiazol-2-yl]benzenesulfonamide; 3], were evaluated in monkeys. Conversion to 1 was low (<3%) with both derivs., and neither entity was an effective prodrug, but the oral bioavailability of 3 (56%) compared with 1 (4%) was significantly improved. The hypothesis that the increased oral bioavailability of 3 was due to a reduction in hydrogen bonding sites in the mol. led to the design of (R)-N-[4-[2-[2-hydroxy-2-(pyridin-2-yl)ethyl]amino]ethyl]phenyl]-4-[4-(4-(trifluoromethyl)phenyl)thiazol-2-yl]benzenesulfonamide (4), a 2-pyridyl β_3 -adrenergic receptor agonist with improved oral bioavailability in rats and monkeys.

IT 479092-32-5

RL: BSU (Biological study, unclassified); PKT (Pharmacokinetics); BIOL (Biological study)

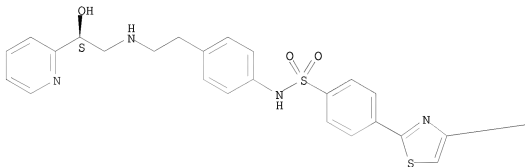
(pharmacokinetics of a thiazole benzenesulfonamide β_3 -adrenergic receptor agonist and its analogs in rats, dogs, and monkeys)

RN 479092-32-5 HCAPLUS

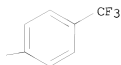
CN Benzenesulfonamide, N-[4-[2-[(2S)-2-hydroxy-2-(2-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[4-(4-(trifluoromethyl)phenyl)-2-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT:

26

THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Updated Search

SearchSTN

L16 ANSWER 23 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:294225 HCAPLUS

DOCUMENT NUMBER: 136:273568

TITLE: Compositions for treating diabetic retinopathy containing a somatostatin and a thyroid-related substance and methods of using same

INVENTOR(S): Grant, Maria

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 11 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20020045569	A1	20020418	US 2001-804484	20010313
US 6852688	B2	20050208		

PRIORITY APPLN. INFO.: US 2000-188483P P 20000310

AB The subject invention provides novel methods and materials for treating diabetic retinopathy. One embodiment of the subject invention involves the co-administration of a somatostatin, or analog thereof, and a thyroid-related substance such as thyroxine. Somatostatin or thyroid-related substance can be administered in combination, or sep. through the same or different modes of administration. A kit comprising at least one container having somatostatin and a thyroid-related substance disposed therein is also claimed, as is an article of manufacture comprising somatostatin and thyroid-related substance.

IT 217480-24-5, L-797591

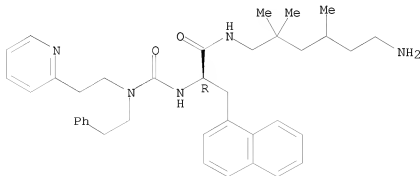
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(compsn. and method for treating diabetic retinopathy using somatostatin and thyroid-related substance)

RN 217480-24-5 HCAPLUS

CN 1-Naphthalenepropanamide, N-(6-amino-2,2,4-trimethylhexyl)- α -[[(2-phenylethyl)[2-(2-pyridinyl)ethyl]amino]carbonyl]amino]-, (α R)- (CA INDEX NAME)

Absolute stereochemistry.



SearchSTN

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 24 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:290504 HCAPLUS

DOCUMENT NUMBER: 137:28062

TITLE: Anti-secretory properties of non-peptide somatostatin receptor agonists in isolated rat colon: luminal activity and possible interaction with p-glycoprotein
Emery, P. T. J.; Higgs, N. B.; Warhurst, A. C.; Carlson, G. L.; Warhurst, G.

AUTHOR(S):
CORPORATE SOURCE: Gut Barrier and Drug Absorption Group, Clinical Division I, Hope Hospital, Salford Royal Hospitals NHS Trust and University of Manchester, Salford, M6 8HD, UK

SOURCE: British Journal of Pharmacology (2002), 135(6), 1443-1448

CODEN: BJPCBM; ISSN: 0007-1188

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 1 The diverse physiol. actions of somatostatin are mediated by a family of G-protein coupled receptors (SSTRs). Several peptide analogs of somatostatin such as octreotide have been developed for therapeutic use, including treatment of gastrointestinal disorders such as secretory diarrhea. However, their development as anti-diarrheal agents has been limited by poor oral bioavailability, necessitating parenteral administration. This in vitro study investigated the anti-secretory potential of a group of novel, non-peptide, somatostatin-receptor agonists that selectively activate specific SSTR subtypes to assess their potential for oral administration. 2 The ability of the agonists to inhibit forskolin-stimulated chloride secretion was measured using a sensitive bioassay system in isolated rat colonic mucosa. 3 The SSTR-2 selective agonist, L-779,976 was 10-times more potent than octreotide as an inhibitor of secretion when added to the basolateral surface of rat colon. Non-peptide agonists selective for SSTR1 (L-797,591), SSTR3 (L-796,778), SSTR4 (L-803,087) or SSTR5 (L-817,818) showed little or no anti-secretory activity in this preparation. 4 L-779,976 was able to inhibit secretion when applied to the luminal surface at sub-micromolar concns. suggesting that it can cross the colonic epithelium. The anti-secretory potency of luminal L-779,976 was increased 3 fold in the presence of GF120918, a known inhibitor of P-glycoprotein. 5 Non-peptide somatostatin receptor agonists may provide a basis for the development of new, orally available anti-diarrheal therapies.

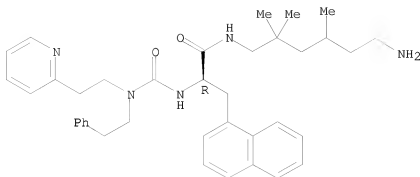
IT 217480-24-5, L797591

RL: PAC (Pharmacological activity); BIOL (Biological study)
(SSTR1 selective agonist; anti-secretory properties of non-peptide somatostatin receptor agonists in isolated rat colon in relation to luminal activity and possible interaction with p-glycoprotein)

RN 217480-24-5 HCAPLUS

CN 1-Naphthalenepropanamide, N-(6-amino-2,2,4-trimethylhexyl)- α -[[[(2-phenylethyl)[2-(2-pyridinyl)ethyl]amino]carbonyl]amino]-, (aR)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 25 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:240217 HCAPLUS

DOCUMENT NUMBER: 137:118909

TITLE: Drug design at peptide receptors: somatostatin receptor ligands

AUTHOR(S): Hannon, Jason P.; Nunn, Caroline; Stolz, Barbara; Bruns, Christian; Weckbecker, Gisbert; Lewis, Ian; Troxler, Thomas; Hurth, Konstanze; Hoyer, Daniel

CORPORATE SOURCE: Nervous System, Novartis Pharma AG, Basel, CH-4002, Switz.

SOURCE: Journal of Molecular Neuroscience (2002), 18(1/2), 15-27

CODEN: JMNES; ISSN: 0895-8696

PUBLISHER: Humana Press Inc.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Somatostatin (SRIF, somatotropin release inhibiting factor), discovered for its inhibitory action on growth hormone (GH) secretion from pituitary, is an abundant neuropeptide. Two forms, SRIF14 and SRIF28 exist. Recently, a second family of peptides with very similar sequences and features was described; the cortistatins (CST), CST17 and CST29 which are brain selective. The five cloned SRIF receptors (sst1-5) belong to the G-protein coupled/heptathelical receptor family. Structural and operational features distinguish two classes of receptors; SRIF1-sst2/sst3/sst5 (high affinity for octreotide or seglitide) and SRIF2-sst1/sst4 (very low affinity for the aforementioned ligands). The affinity of SRIF receptors for somatostatins and cortistatins is equally high, and it is not clear whether selective receptors do exist for one or the other of the peptides. Several radiologands label all SRIF receptors, e.g., [125I] LTT-SRIF28, [125I] CGP23996, [125I] Tyr10cortistatin or [125I] Tyr11SRIF14. In contrast, [125I] Tyr3octreotide, [125I] BIM23027, [125I] MK678 or [125I] D-Trp8SRIF14 label predominantly SRIF1 sites, especially sst2 and possibly sst5 receptors. In brain, [125I]Tyr3octreotide binding equates with sst2 receptor mRNA distribution. Native SRIF2 receptors can be labeled with [125I]SRIF14 in the presence of high NaCl in brain (sst1) or lung (sst4) tissue. Short cyclic or linear peptide analogs show selectivity for sst2/sst5 (octreotide, lanreotide, BIM 23027), sst1 (CH-275), sst3 (sst3-ODN-8), or sst5 receptors (BIM 23268); although claims for selectivity have not

always been confirmed. Beta peptides with affinity for SRIF receptors are also reported. The general lack of SRIF receptor antagonists is unique for peptide receptors, although CYN 154806 is a selective and potent sst2 antagonist. Nonpeptide ligands are still rare, although a number of mols. have been reported with selectivity and potency for sst1 (L757,519), sst2 (L779,976), sst3 (L796,778), sst4 (NNC 26-9100, L803,087) or sst1/sst5 receptors (L817,018). Such mols. are essential to establish the role of SRIF receptors, e.g., sst1 in hypothalamic glutamate currents: sst2 in inhibiting release of GH, glucagon, TSH, gastric acid secretion, pain, seizures and tumor growth, and sst5 in vascular remodeling and inhibition of insulin and GH release.

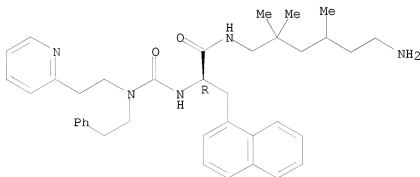
IT 217480-24-5

RL: PAC (Pharmacological activity); BIOL (Biological study)
(drug design at peptide receptors for somatostatin receptor ligands)

RN 217480-24-5 HCAPLUS

CN 1-Naphthalenepropanamide, N-(6-amino-2,2,4-trimethylhexyl)- α -[[[(2-phenylethyl)[2-(2-pyridinyl)ethyl]amino]carbonylamino]-, (aR)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 26 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:758189 HCAPLUS

DOCUMENT NUMBER: 136:78833

TITLE: Formation, Characterization, and Reactivity of Bis(μ -oxo)dinickel(III) Complexes Supported by A Series of Bis[2-(2-pyridyl)ethyl]amine Ligands
AUTHOR(S): Itoh, Shinobu; Bandoh, Hideki; Nakagawa, Motonobu; Nagatomo, Shigenori; Kitagawa, Teizo; Karlin, Kenneth D.; Fukuzumi, Shunichi

CORPORATE SOURCE: Department of Chemistry Graduate School of Science, Osaka City University, Sumiyoshi-ku Osaka, 558-8585, Japan

SOURCE: Journal of the American Chemical Society (2001), 123(45), 11168-11178

PUBLISHER: CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: American Chemical Society

LANGUAGE: Journal

English

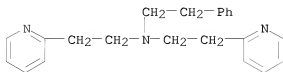
OTHER SOURCE(S): CASREACT 136:78833

AB Bis(μ -oxo)dinickel(III) complexes supported by bis[2-(2-pyridyl)ethyl]amine ligands were successfully generated by treating the corresponding bis(μ -hydroxo)dinickel(II) complexes or bis(μ -methoxo)dinickel(II) complex with an equimolar amount of H₂O₂ in acetone at low temperature. The bis(μ -oxo)dinickel(III) complexes exhibit a characteristic UV-visible absorption band at approx. 410 nm and a resonance Raman band at 600-610 cm⁻¹ that shifted to 570-580 cm⁻¹ upon 180-substitution. Kinetic studies and isotope labeling expts. using 18O₂ imply the existence of intermediate(s) such as peroxo dinickel(II) in formation of the bis(μ -oxo)dinickel(III) complex. The bis(μ -oxo)dinickel(III) complexes supported by the mononucleating ligands (L1X = para-substituted N,N-bis[2-(2-pyridyl)ethyl]-2-phenylethylamine; X = OMe, Me, H, Cl) gradually decompose, leading to benzylic hydroxylation of the ligand side arm (phenethyl group). The kinetics of the ligand hydroxylation process including kinetic D isotope effects (KIE), p-substituent effects (Hammett plot), and activation parameters (Δ H[‡].thermod. and Δ S[‡].thermod.) indicate that the bis(μ -oxo)dinickel(III) complex exhibits an ability of H atom abstraction from the substrate moiety as in the case of the bis(μ -oxo)dnicopper(III) complex. Such a reactivity of bis(μ -oxo)dinickel(III) complexes also was suggested by the observed reactivity toward external substrates such as phenol derivs. and 1,4-cyclohexadiene. The thermal stability of the bis(μ -oxo)dinickel(III) complex is significantly enhanced when the dinucleating ligand with a longer alkyl strap is adopted instead of the mononucleating ligand. In the m-xylyl ligand system, no aromatic ligand hydroxylation occurred, showing a sharp contrast with the reactivity of the (μ - η^2 : η^2 -peroxo)dnicopper(II) complex with the same ligand which induces aromatic ligand hydroxylation via an electrophilic aromatic substitution mechanism. Differences in the structure and reactivity of the active O complexes between the Ni and the Cu systems are discussed from the detailed comparison of these two systems with the same ligand.

IT 31582-30-6
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reactant for preparation of nickel hydroxide pyridylethylaminomethylbenzene dinuclear complex)

RN 31582-30-6 HCAPLUS

CN 2-Pyridineethanamine, N-(2-phenylethyl)-N-[2-(2-pyridinyl)ethyl]- (CA INDEX NAME)



REFERENCE COUNT: 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 27 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2001:178682 HCAPLUS
 DOCUMENT NUMBER: 134:261408

SearchSTN

TITLE: Somatostatin receptor subtype 1 (sst1) regulates intracellular 3',5'-cyclic adenosine monophosphate accumulation in rat embryonic cortical neurons: evidence with L-797,591, an sst1-subtype-selective nonpeptidyl agonist

AUTHOR(S): Blake, A. D.

CORPORATE SOURCE: Merck Research Laboratories, Rahway, NJ, 07065, USA

SOURCE: Neuropharmacology (2001), 40(4), 590-596
CODEN: NEPHBW; ISSN: 0028-3908

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

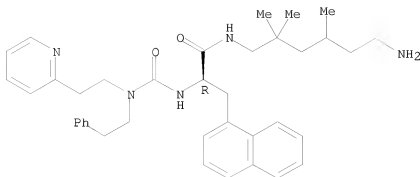
AB Somatostatin (SRIF) initiates its biol. activities by interacting with five homologous G-protein-coupled receptor subtypes (sst1-5). In the mammalian nervous system, sst1-5 receptor mRNA expression patterns have been localized by in situ hybridization studies, or at the protein level with receptor-specific antibodies. Cortical responses to SRIF have been demonstrated, although a functional relationship between an SRIF effect and an individual receptor subtype is lacking. The recent development of novel, subtype-selective SRIF receptor ligands now provides a means to correlate receptor subtype expression patterns with the corresponding biol. function. In cultured monolayers of E17-18 rat embryonic cortical neurons, 10⁻⁷ M SRIF-28 inhibited 10⁻⁶ M forskolin-stimulated cAMP accumulation by 37%, a level of inhibition that was mimicked by L-797,591, a potent sst1-selective agonist. SRIF-14 or L-797,591 inhibited forskolin-stimulated cAMP accumulation in a concentration-dependent fashion, with EC50s (effective concentration for 50% maximal response) of 8.0 + 10⁻¹⁰ M and 7.0 + 10⁻¹⁰ M, resp. No similar concentration-dependent effect on forskolin-stimulated cAMP levels was observed with sst2-, sst3- or sst4-selective agonists. Furthermore, both SRIF-14 and L-797,591 inhibited 10⁻⁷ M CRH-induced cAMP in the embryonic neurons. These results are the first evidence demonstrating that sst1 regulates intracellular cAMP levels in embryonic neurons and may inhibit CRH-mediated effects in the embryonic cortex.

IT 217480-24-5, L-797591
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(somatostatin receptor subtype 1 regulates intracellular cAMP accumulation in rat embryonic cortical neurons in relation to evidence with L-797,591, sst1-subtype selective nonpeptidyl agonist)

RN 217480-24-5 HCAPLUS

CN 1-Naphthalenepropanamide, N-(6-amino-2,2,4-trimethylhexyl)-α-[[[(2-phenylethyl)[2-(2-pyridinyl)ethyl]amino]carbonyl]amino]-, (αR)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 28 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:54871 HCAPLUS

DOCUMENT NUMBER: 134:237062

TITLE: Parallel synthesis of tertiary amines using polystyrene sulfonyl chloride (PS-TsCl) resin
 AUTHOR(S): Hu, Yonghan; Gooding, Owen W.; Labadie, Jeff W.; Miller, Wendy; Porco, John A., Jr.
 CORPORATE SOURCE: Argonaut Technologies, San Carlos, CA, 94070, USA
 SOURCE: Proceedings of ECSOC-1: The First International Electronic Conference on Synthetic Organic Chemistry; [and] Proceedings of ECSOC-2: The Second International Electronic Conference on Synthetic Organic Chemistry, Sept. 1-30, 1997, 1998 (1999), Meeting Date 1997-1998, 140-144. Editor(s): Lin, Shu-Kun; Pombo-Villar, Esteban. Molecular Diversity Preservation International: Basel, Switz.
 CODEN: 69ASBO

DOCUMENT TYPE: Conference; (computer optical disk)

LANGUAGE: English

OTHER SOURCE(S): CASREACT 134:237062

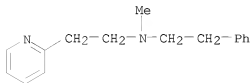
AB A focused library of tertiary amines was synthesized by reacting alcs. with polystyrene sulfonyl chloride resin to give polystyrene sulfonates, which were then reacted with secondary amines to give tertiary amines.

IT 110439-26-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (parallel synthesis of tertiary amines using polystyrene sulfonyl chloride resin)

RN 110439-26-4 HCAPLUS

CN 2-Pyridineethanamine, N-methyl-N-(2-phenylethyl)- (CA INDEX NAME)



SearchSTN

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 29 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:1361 HCAPLUS

DOCUMENT NUMBER: 134:157627

TITLE: Identification and characterization of subtype selective somatostatin receptor agonists

AUTHOR(S): Rohrer, Susan P.; Schaeffer, James M.

CORPORATE SOURCE: Department of Endocrinology and Chemical Biology, Merck Research Laboratories, Rahway, NJ, 07065, USA

SOURCE: Journal of Physiology (Paris) (2000), 94(3-4), 211-215
CODEN: JHYSEM; ISSN: 0928-4257

PUBLISHER: Editions Scientifiques et Medicales Elsevier

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 11 refs. High affinity, subtype selective non-peptide agonists of somatostatin receptor subtypes 1-5 were identified in combinatorial libraries constructed based on mol. modeling of known peptide agonists. Simultaneous traditional chemical synthesis yielded an addnl. series of somatostatin subtype-2 receptor (SSTR2) selective agonists. These compds. have been used to further define the physiol. functions of the individual somatostatin receptor subtypes. In vitro expts. demonstrated the role of the SSTR2 in inhibition of glucagon release from mouse pancreatic α -cells and the somatostatin subtype-5 receptor (SSTR5) as a mediator of insulin secretion from pancreatic β -cells. Both SSTR2 and SSTR5 regulated growth hormone release from the rat anterior pituitary gland. In vivo studies performed with SSTR2 receptor selective compds. demonstrated effective inhibition of pulsatile growth hormone release in rats. The SSTR2 selective compds. also lowered plasma glucose levels in normal and diabetic animal models. The availability of high affinity, subtype selective non-peptide agonists for each of the somatostatin receptors provides a direct approach to defining their physiol. function both peripherally and in the central nervous system.

IT 217480-24-5, L 797591

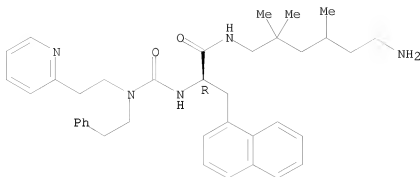
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(identification and characterization of subtype selective somatostatin receptor agonists)

RN 217480-24-5 HCAPLUS

CN 1-Naphthalenepropanamide, N-(6-amino-2,2,4-trimethylhexyl)- α -[[[(2-phenylethyl)[2-(2-pyridinyl)ethyl]amino]carbonyl]amino]-, (α R)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 30 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:368337 HCAPLUS

DOCUMENT NUMBER: 133:4656

TITLE: Preparation of heteroarylpyrazoles as p38 kinase inhibitors

INVENTOR(S): Anantanarayan, Ashok; Clare, Michael; Collins, Paul W.; Crich, Joyce Z.; Devraj, Rajesh; Flynn, Daniel L.; Geng, Lifeng; Graneto, Matthew J.; Hanau, Cathleen E.; Hanson, Gunnar J.; Hartmann, Susan J.; Hepperle, Michael; Huang, He; Khanna, Ish K.; Koszyk, Francis J.; Liao, Shuyuan; Metz, Suzanne; Partis, Richard A.; Perry, Thao D.; Rao, Shashidhar N.; Selness, Shaun Raj; South, Michael S.; Stealey, Michael A.; Talley, John Jeffrey; Vazquez, Michael L.; Weier, Richard M.; Xu, Xiangdong; Yu, Yi

PATENT ASSIGNEE(S): G.D. Searle and Co., USA

SOURCE: PCT Int. Appl., 1210 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000031063	A1	20000602	WO 1999-US26007	19991117
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6514977	B1	20030204	US 1998-196623	19981120
CA 2351725	A1	20000602	CA 1999-2351725	19991117
EP 1144403	A1	20011017	EP 1999-965756	19991117
EP 1144403	B1	20041006		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

SearchSTN

IE, SI, LT, LV, FI, RO

BR 9915420	A	20020122	BR 1999-15420	19991117
EE 200100268	A	20021216	EE 2001-268	19991117
NZ 512344	A	20031128	NZ 1999-512344	19991117
AU 774262	B2	20040624	AU 2000-21454	19991117
AT 278685	T	20041015	AT 1999-965756	19991117
ES 2229809	T3	20050416	ES 1999-965756	19991117
US 6525059	B1	20030225	US 2000-513351	20000224
MX 2001PA05043	A	20010710	MX 2001-PA5043	20010518
NO 2001002456	A	20010719	NO 2001-2456	20010518
BG 105620	A	20020131	BG 2001-105620	20010619
HK 1040705	A1	20050304	HK 2002-102213	20020322
AU 2003200580	A1	20030501	AU 2003-200580	20030217

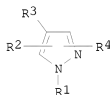
PRIORITY APPLN. INFO.:

US 1998-196623	A	19981120
US 1997-47570P	P	19970522
AU 1998-75883	A3	19980522
US 1998-83670	A2	19980522
WO 1999-US26007	W	19991117

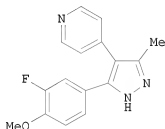
OTHER SOURCE(S):

MARPAT 133:4656

GI



I



II

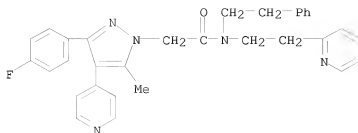
AB Title compds. [I; R1 = H, OH, NH2, (cyclo)alk(en)yl, acyl, aryl, etc.; R2 = H, halo, alkyl, alkoxy, (un)substituted piperidinyl, etc.; R3 = pyridyl, pyrimidinyl, quinolyl, etc.; R4 = H, alkyl, heterocyclyl, aryl, etc.] were prepared by reaction of ketones with hydrazines. Thus, R3CH2C(=O)R3 (R3 = 4-pyridinyl) was condensed with 3,4-F(MeO)C6H3CHO and the product cyclocondensed with TsNHNH2 to give title compound II. Data for biol. activity of I were given.

IT 216528-02-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of heteroarylpyrazole p38 kinase inhibitors by cyclocondensation of hydrazines with ketones)

RN 216528-02-8 HCAPLUS

CN 1H-Pyrazole-1-acetamide, 3-(4-fluorophenyl)-5-methyl-N-(2-phenylethyl)-4-(4-pyridinyl)-N-[2-(2-pyridinyl)ethyl]- (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 31 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:126020 HCAPLUS

DOCUMENT NUMBER: 132:302518

TITLE: Reaction of Cu(I) complexes bearing a phenol group in the ligand with O₂

AUTHOR(S): Itoh, S.; Hashimoto, Y.; Fukuzumi, S.

CORPORATE SOURCE: Graduate School of Engineering, Department of Material and Life Science, Osaka University, Suita, Osaka, Japan

SOURCE: Applied Catalysis, A: General (2000), 194-195, 453-461
CODEN: ACAGE4; ISSN: 0926-860X

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Reactions of dioxygen and Cu(I) complexes of bis[2-(2-pyridyl)ethyl]amine ligands bearing different phenol groups (2H = N,N-bis[2-(2-pyridyl)ethyl]-2-(3-hydroxyphenyl)ethylamine, 3H = N,N-bis[2-(2-pyridyl)ethyl]tyramine, 4H = N,N-bis[2-(2-pyridyl)ethyl]-2-(2-hydroxy-5-methylphenyl)ethylamine) were studied to obtain insight into the reactivity of Cu-active O complexes toward phenols. Treatment of [CuI(2H)](PF₆) and [CuI(3H)](PF₆) with O₂ resulted in the benzylic ligand hydroxylation in 9 and 14%, resp., together with formation of polymeric products, while the reaction of [CuI(4H)](PF₆) and O₂ gave a dinuclear phenolate Cu(II) complex, [CuII(4-)₂]²⁺, and H₂O₂. The structure and reactivity of the active O intermediates are discussed.

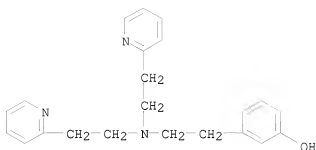
IT 264224-84-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(for preparation of copper bis(pyridylethyl)((hydroxyphenyl)ethyl)amine and -((hydroxymethylphenyl)ethyl)amine complexes)

RN 264224-84-2 HCAPLUS

CN Phenol, 3-[2-[bis[2-(2-pyridinyl)ethyl]amino]ethyl]- (CA INDEX NAME)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 32 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:574186 HCAPLUS

DOCUMENT NUMBER: 131:328077

TITLE: Aliphatic Hydroxylation by a Bis(μ-oxo)nickel(III) Complex

AUTHOR(S): Itoh, Shinobu; Bandoh, Hideki; Nagatomo, Shigenori; Kitagawa, Teizo; Fukuzumi, Shunichi

CORPORATE SOURCE: Department of Material and Life Science Graduate School of Engineering, Osaka University, Suita Osaka, 565-0871, Japan

SOURCE: Journal of the American Chemical Society (1999), 121(38), 8945-8946

CODEN: JACSAT; ISSN: 0002-7863

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

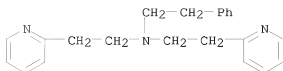
AB Bis(μ-hydroxo)nickel(III) complexes of tridentate ligands LX $\{(\text{C}_5\text{H}_4\text{N}(\text{CH}_2)_2)_2\text{N}(\text{CH}_2)_2\text{C}_6\text{H}_4\text{-p-X}; \text{X} = \text{OMe, Me, H, Cl}\}$ were prepared as starting materials by reacting the ligand with $\text{Ni}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ in the presence of triethylamine. Addition of 1 equiv of H_2O_2 into an acetone solution of $[(\text{LXNiIII})_2(\mu\text{-OH})_2]^{2+}$ at a low temperature (-90°C) resulted in a bis(μ-oxo)nickel(III) complexes with a rate constant (kf) of 0.14 s^{-1} at -90°C and activation parameters $\Delta\text{H}^\ddagger_{\text{thermod.}} = 5.6 \pm 0.1 \text{ kcal mol}^{-1}$ and $\Delta\text{S}^\ddagger_{\text{thermod.}} = -30.9 \pm 0.6 \text{ cal K}^{-1} \text{ mol}^{-1}$. The bis(μ-oxo)nickel(III) complexes gradually decompose at higher temperature (above -50°C) leading to benzylic ligand hydroxylation to give LXOH, obeying first-order kinetics with the activation parameters $\Delta\text{H}^\ddagger_{\text{thermod.}} = 14.9 \pm 0.2 \text{ kcal mol}^{-1}$ and $\Delta\text{S}^\ddagger_{\text{thermod.}} = -10.1 \pm 0.8 \text{ cal K}^{-1} \text{ mol}^{-1}$. Ligand hydroxylation in $[(\text{LXNiIII})_2(\mu\text{-O})_2]^{2+}$ likely proceeds via the rate-determining hydrogen abstraction, followed by hydroxyl rebound as determined from deuterium isotope effect expts. and a Hammett plot of p-substituent effects.

IT 31582-30-6

RL: RCT (Reactant); RACT (Reactant or reagent)
(for preparation of bis(pyridylethyl)phenylethylamine bis(μ-hydroxo)nickel(II) complex)

RN 31582-30-6 HCAPLUS

CN 2-Pyridineethanamine, N-(2-phenylethyl)-N-[2-(2-pyridinyl)ethyl]- (CA INDEX NAME)



L16 ANSWER 33 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:789144 HCAPLUS

DOCUMENT NUMBER: 130:38377

TITLE: Preparation of heteroarylpyrazoles as p38 kinase inhibitors

INVENTOR(S): Anantanarayan, Ashok; Clare, Michael; Collins, Paul W.; Crich, Joyce Zuowu; Devraj, Rajesh; Flynn, Daniel L.; Geng, Lifeng; Hanson, Gunnar J.; Koszyk, Francis J.; Liao, Shuyuan; Partis, Richard A.; Rao, Shashidhar N.; Selness, Shaun Raj; South, Michael S.; Stealey, Michael A.; Weier, Richard M.; Xu, Xiangdong

PATENT ASSIGNEE(S): G.D. Searle and Co., USA; et al.

SOURCE: PCT Int. Appl., 828 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

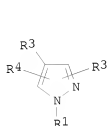
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
WO 9852940	A1	19981126	WO 1998-US10436	19980522
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LI, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2291115	A1	19981126	CA 1998-2291115	19980522
AU 9875883	A	19981211	AU 1998-75883	19980522
AU 754830	B2	20021128		
ZA 9804358	A	19990524	ZA 1998-4358	19980522
EP 1000055	A1	20000517	EP 1998-923642	19980522
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200000235	T2	20000522	TR 2000-235	19980522
EE 9900527	A	20000615	EE 1999-527	19980522
BR 9809147	A	20000801	BR 1998-9147	19980522
HU 2000001880	A2	20010328	HU 2000-1880	19980522
HU 2000001880	A3	20020328		
JP 2002508754	T	20020319	JP 1998-550650	19980522
NZ 501112	A	20021025	NZ 1998-501112	19980522
AP 1246	A	20040207	AP 1999-1715	19980522
W: GM, GH, KE, LS, MW, SD, SZ, UG, ZW				
IL 132991	A	20051120	IL 1998-132991	19980522

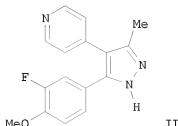
SearchSTN

NO 9905695	A	20000121	NO 1999-5695	19991119
MX 9910759	A	20000531	MX 1999-10759	19991122
BG 64313	B1	20040930	BG 1999-103964	19991208
AU 2003200580	A1	20030501	AU 2003-200580	20030217
PRIORITY APPLN. INFO.:			US 1997-47570P	P 19970522
			AU 1998-75883	A3 19980522
			WO 1998-US10436	W 19980522

OTHER SOURCE(S): MARPAT 130:38377
GI



I



II

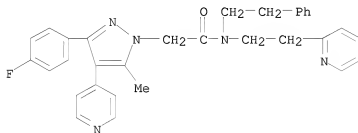
AB Title compds. [I; R1 = H, NH2, (cyclo)alk(en)yl, acyl, aryl, etc.; R2 = H, halo, alkyl, alkoxy, etc.; R3 = pyridyl, pyrimidinyl, quinolyl, etc.; R4 = H, alkyl, heterocyclyl, aryl, etc.] were prepared Thus, R3CH2COMe (R3 = 4-pyridinyl) was condensed with 3,4-F(MeO)C6H3CHO and the product cyclocondensed with TsNHNH2 to give title compound II. Data for biol. activity of I were given.

IT 216528-02-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heteroarylpyrazoles as p38 kinase inhibitors)

RN 216528-02-8 HCAPLUS

CN 1H-Pyrazole-1-acetamide, 3-(4-fluorophenyl)-5-methyl-N-(2-phenylethyl)-4-(4-pyridinyl)-N-[2-(2-pyridinyl)ethyl]- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 34 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:775150 HCAPLUS

DOCUMENT NUMBER: 130:105498

Updated Search

SearchSTN

TITLE: Rapid identification of subtype-selective agonists of the somatostatin receptor through combinatorial chemistry. [Erratum to document cited in CA130:47679]

AUTHOR(S): Rohrer, Susan P.; Birzin, Elizabeth T.; Mosley, Ralph T.; Berk, Scott C.; Hutchins, Steven M.; Shen, Dong-Ming; Xiong, Yusheng; Hayes, Edward C.; Parmar, Rupa M.; Foor, Forrest

CORPORATE SOURCE: Dep. Cell Biochemistry and Physiology, Merck Res. Lab., Rahway, NJ, 07065, USA

SOURCE: Science (Washington, D. C.) (1998), 282(5394), 1646
CODEN: SCIEAS; ISSN: 0036-8075

PUBLISHER: American Association for the Advancement of Science

DOCUMENT TYPE: Journal

LANGUAGE: English

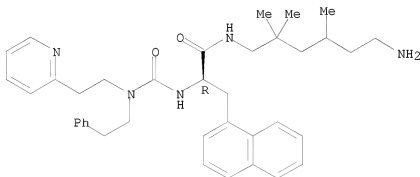
AB In the third line of the legend of Table 1 (page 738), "(in nanomoles)" should have read "(nM)". In the first footnote in the legend of Table 2 (page 739), "(in M)" should have read, "(nM)".

IT 217480-24-5, L 797591
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(somatostatin receptor subtype-selective agonist rapid identification through combinatorial chemical and receptor involvement in pancreatic and growth hormone secretion regulation (Erratum))

RN 217480-24-5 HCAPLUS

CN 1-Naphthalenepropanamide, N-(6-amino-2,2,4-trimethylhexyl)- α -[[[(2-phenylethyl)[2-(2-pyridinyl)ethyl]amino]carbonyl]amino]-, (α R)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 35 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:697962 HCAPLUS

DOCUMENT NUMBER: 130:47679

TITLE: Rapid identification of subtype-selective agonists of the somatostatin receptor through combinatorial chemistry

AUTHOR(S): Rohrer, Susan P.; Birzin, Elizabeth T.; Mosley, Ralph T.; Berk, Scott C.; Hutchins, Steven M.; Shen,

Updated Search

Dong-Ming; Xiong, Yusheng; Hayes, Edward C.; Parmar, Rupa M.; Foor, Forrest; Mitra, Sudha W.; Degrado, Sylvia J.; Shu, Min; Klopp, John M.; Cai, Sheng-Jian; Blake, Allan; Chan, Wanda W. S.; Pasternak, Alex; Yang, Lihu; Patchett, Arthur A.; Smith, Roy G.; Chapman, Kevin T.; Schaeffer, James M.

CORPORATE SOURCE: Dep. Cell Biochemistry and Physiology, Merck Res. Lab., Rahway, NJ, 07065, USA

SOURCE: Science (Washington, D. C.) (1998), 282(5389), 737-740
CODEN: SCIEAS; ISSN: 0036-8075

PUBLISHER: American Association for the Advancement of Science

DOCUMENT TYPE: Journal

LANGUAGE: English

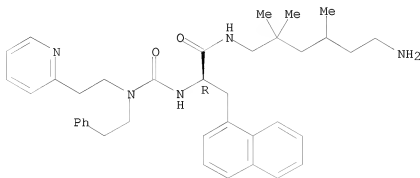
AB Nonpeptide agonists of each of the five somatostatin receptors were identified in combinatorial libraries constructed on the basis of mol. modeling of known peptide agonists. In vitro expts. using these selective compds. demonstrated the role of the somatostatin subtype-2 receptor in inhibition of glucagon release from mouse pancreatic alpha cells and the somatostatin subtype-5 receptor as a mediator of insulin secretion from pancreatic beta cells. Both receptors regulated growth hormone release from the rat anterior pituitary gland. The availability of high-affinity, subtype-selective agonists for each of the somatostatin receptors provides a direct approach to defining their physiol. functions.

IT 217480-24-5, L 797591
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(somatostatin receptor subtype-selective agonist rapid identification through combinatorial chemical and receptor involvement in pancreatic and growth hormone secretion regulation)

RN 217480-24-5 HCAPLUS

CN 1-Naphthalenepropanamide, N-(6-amino-2,2,4-trimethylhexyl)- α -[[[(2-phenylethyl)[2-(2-pyridinyl)ethyl]amino]carbonyl]amino]-, (α R)- (CA INDEX NAME)

Absolute stereochemistry.

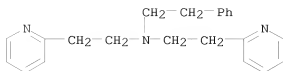


REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 36 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:269135 HCAPLUS

SearchSTN

DOCUMENT NUMBER: 128:262408
 ORIGINAL REFERENCE NO.: 128:51857a,51860a
 TITLE: Mechanistic Studies of Aliphatic Ligand Hydroxylation of a Copper Complex by Dioxxygen: A Model Reaction for Copper Monooxygenases
 AUTHOR(S): Itoh, Shinobu; Nakao, Hajime; Berreau, Lisa M.; Kondo, Toshihiko; Komatsu, Mitsuo; Fukuzumi, Shunichi
 CORPORATE SOURCE: Department of Applied Chemistry Faculty of Engineering, Osaka University, Suita, 565, Japan
 SOURCE: Journal of the American Chemical Society (1998), 120(12), 2890-2899
 CODEN: JACSAT; ISSN: 0002-7863
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Mechanistic studies on the aliphatic ligand hydroxylation in a Cu complex of tridentate ligand (1a) {N,N-bis[2-(2-pyridyl)ethyl]-2-phenylethylamine} by O₂ were performed to shed light on the structure and reactivity of the active O species of the authors' functional model for Cu monooxygenases (J. Am. Chemical Society 1995, 117, 4714). When the Cu complex [CuI(1a)(ClO₄)₂] was treated with an equimolar amount of benzoin and NET₃ in CH₂Cl₂ under O₂ atmosphere, efficient hydroxylation occurred selectively at the benzylic position of the ligand to provide oxygenated product (2a) {N,N-bis[2-(2-pyridyl)ethyl]-2-phenyl-2-hydroxyethylamine} quant. An isotope labeling experiment using 18O₂ confirms that the O atom of the OH group in 2a originates from O₂. Spectroscopic analyses using UV-visible, resonance Raman, and ESR on the reaction of [CuI(1a)]⁺ and O₂ at low temperature show that a μ - η : η 2-peroxodicopper(II) complex is an initially formed intermediate. Kinetic anal. on the peroxo complex formation indicates that the reaction of the Cu(I) complex and the monomeric superoxocopper(II) species is rate-determining for the formation of the μ - η : η 2-peroxodicopper(II) intermediate. When ligand 1a is replaced by 1,1,2,2-tetradeuterated phenethylamine derivative (1a-d₄), a relatively small kinetic D isotope effect (kH/kD = 1.8 at -40°) is observed for the ligand hydroxylation step. The rate of the hydroxylation step is rather insensitive to the p-substituent of the ligand [(PyCH₂CH₂)₂NCH₂CH₂Ar, 1a Ar = C₆H₅; 1b Ar = p-CH₃C₆H₄, 1c Ar = p-ClC₆H₄, and 1d Ar = p-NO₂C₆H₄], but it varies depending on the solvent (THF > acetone > MeOH > CH₂Cl₂). The p-substituent, the solvent, and the kinetic D isotope effects suggest that O-O bond homolysis of the μ - η : η 2-peroxodicopper(II) intermediate is involved as a rate-determining step in the aliphatic ligand hydroxylation process. Based on the results of the kinetics and the crossover expts., a mechanism is proposed involving intramol. C-H bond activation in a bis- μ -oxodicopper(III) type intermediate for the ligand hydroxylation reaction.
 IT 31582-30-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (for preparation of copper amine perchlorate complex followed by selective ligand hydroxylation)
 RN 31582-30-6 HCAPLUS
 CN 2-Pyridineethanamine, N-(2-phenylethyl)-N-[2-(2-pyridinyl)ethyl]- (CA INDEX NAME)



REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 37 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1995:508373 HCAPLUS

DOCUMENT NUMBER: 123:279601

ORIGINAL REFERENCE NO.: 123:49923a,49926a

TITLE: Functional Model of Dopamine β -Hydroxylase.
Quantitative Ligand Hydroxylation at the Benzylic
Position of a Copper Complex by Dioxygen

AUTHOR(S): Itoh, Shinobu; Kondo, Toshihiko; Komatsu, Mitsuo;
Ohshiro, Yoshiki; Li, Chunmin; Kanehisa, Nobuko; Kai,
Yasushi; Fukuzumi, Shunichi

CORPORATE SOURCE: Faculty of Engineering, Osaka University, Suita, 565,
Japan

SOURCE: Journal of the American Chemical Society (1995),
117(16), 4714-15

CODEN: JACSAT; ISSN: 0002-7863

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

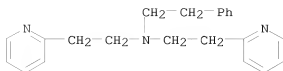
AB A functional model of dopamine β -hydroxylase (D β H) has been reported using a copper complex with a tridentate ligand Py2Phe (N,N-bis[2-(2-pyridyl)ethyl]-2-phenylethylamine). When copper complex [Cu(II)(Py2Phe)(ClO4)2] (I), was treated with an equimolar amount of benzoin and triethylamine in CH2Cl2 under O2 atmosphere, the quant. hydroxylation occurred selectively at the benzylic position of the ligand. The crystal structure of the Cu(II) complex of the hydroxylated ligand as well as that of the starting material I has been determined. The oxygen source of the ligand hydroxylation was confirmed to be mol. oxygen by the quant. incorporation of 18O when the reaction was carried out under 18O2. The stoichiometry of O2 to copper was determined to be 1:1 by manometry. When the Py2Phe ligand was treated with [Cu(I)(CH3CN)4]PF6 acting also as a reductant instead of benzoin and triethylamine under O2, the yield of hydroxylation was 50% based on the Cu ion and the stoichiometry of Cu:O2 was 2:1. These results clearly indicate that two equivalent of electrons and one equivalent of O2 are required for the quant. ligand hydroxylation. The mechanism of the present hydroxylation reaction is also discussed.

IT 31582-30-6

RL: RCT (Reactant); RACT (Reactant or reagent)
(tridentate ligand; functional model of dopamine β -hydroxylase
with quant. ligand hydroxylation at benzylic position of a copper
complex by dioxygen)

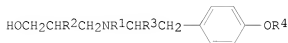
RN 31582-30-6 HCAPLUS

CN 2-Pyridineethanamine, N-(2-phenylethyl)-N-[2-(2-pyridinyl)ethyl]- (CA
INDEX NAME)



L16 ANSWER 38 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 1990:234956 HCAPLUS
 DOCUMENT NUMBER: 112:234956
 ORIGINAL REFERENCE NO.: 112:39621a,39624a
 TITLE: Preparation of (phenylalkyl)propanolamine derivatives
 as antidiabetics as antiobesity agents
 INVENTOR(S): Kienzle, Frank
 PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Switz.
 SOURCE: Eur. Pat. Appl., 14 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 345591	A1	19891213	EP 1989-109675	19890530
EP 345591	B1	19930331		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FI 8902341	A	19891211	FI 1989-2341	19890516
AT 87610	T	19930415	AT 1989-109675	19890530
ES 2053866	T3	19940801	ES 1989-109675	19890530
ZA 8904210	A	19900328	ZA 1989-4210	19890602
AU 8936026	A	19891214	AU 1989-36026	19890605
AU 622907	B2	19920430		
HU 55344	A2	19910528	HU 1989-2868	19890605
JP 02036158	A	19900206	JP 1989-144282	19890608
DK 8902842	A	19891211	DK 1989-2842	19890609
NO 8902387	A	19891211	NO 1989-2387	19890609
NO 170011	B	19920525		
NO 170011	C	19920902		
US 5045567	A	19910903	US 1990-608610	19901031
PRIORITY APPLN. INFO.:			CH 1988-2245	A 19880610
			EP 1989-109675	A 19890530
			US 1989-363242	B1 19890608
OTHER SOURCE(S):	MARPAT 112:234956			
GI				



I

AB The title compds. I [R¹ = H or CH₂CHR⁵(CH₂)nOH, R⁵ = Ph, m-halophenyl, m-F₃CC₆H₄, thienyl, or pyridyl; R² = R⁵; R³ = H, Me; R⁴ = H, HO₂CCH₂,

SearchSTN

Cl-4 alkoxy carbonylmethyl, Cl-4 alkoxyethyl, or Ph Cl-4 alkoxyethyl) and their compatible physiol. salts having a catabolic effect are prepared for use in the treatment of obesity, diabetes mellitus, conditions involving increased protein degradation, and as food additives for obese animals. Thus, di-Et phenylmalonate in diglyme was treated with p-(2-ethoxyethoxy)phenethylamine, the solution stirred 48 h at 95°, cooled, the solvent removed, and the residue chromatog. purified to give Et [[p-(2-ethoxyethoxy)phenethyl]carbonyl]phenyl]acetate (II). The effects of II on the O consumption of albino rats showed its effectiveness in treating obesity.

IT 127298-11-7P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as antidiabetic and antiobesity agent)

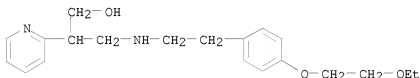
RN 127298-11-7 HCAPLUS

CN 2-Pyridineethanol, β-[[[2-[4-(2-ethoxyethoxy)phenyl]ethyl]amino]methyl]-, ethanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 127298-10-6

CMF C20 H28 N2 O3



CM 2

CRN 144-62-7

CMF C2 H2 O4



L16 ANSWER 39 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1989:593898 HCAPLUS

DOCUMENT NUMBER: 111:193898

ORIGINAL REFERENCE NO.: 111:32219a,32222a

TITLE: Pyridine nucleus hydroxylation with copper oxygenase models

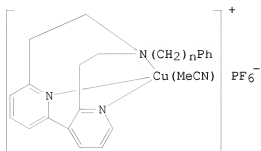
AUTHOR(S): Reglier, Marius; Amadei, Edith; Tadayoni, Rahim; Waegell, Bernard

CORPORATE SOURCE: Lab. Stereochim., Fac. Sci. St. Jerome, Marseille, 13397, Fr.

SOURCE: Journal of the Chemical Society, Chemical Communications (1989), (8), 447-50

SearchSTN

DOCUMENT TYPE: JCCCAT; ISSN: 0022-4936
LANGUAGE: Journal
OTHER SOURCE(S): English
GI CASREACT 111:193898



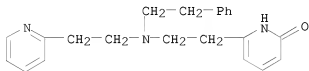
I

AB The reaction of Cu complexes I ($n = 1, 2$) with PhIO resulted in hydroxylation at the 2-position of one pyridine ring. $Cu(III):O$ species was postulated.

IT 123136-36-7P
RL: SPN (Synthetic preparation); PREP (Preparation of preparation of)

RN 123136-36-7 HCAPLUS

CN 2(1H)-Pyridinone, 6-[2-[(2-phenylethyl)[2-(2-pyridinyl)ethyl]amino]ethyl]- (CA INDEX NAME)



L16 ANSWER 40 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1989:553338 HCAPLUS

DOCUMENT NUMBER: 111:153338

ORIGINAL REFERENCE NO.: 111:25553a,25556a

TITLE: Preparation of N-(Fluoroethyl)anilines and heterocyclic analogs as insecticides, acaricides, and microbicides

INVENTOR(S): Hayase, Yoshio; Ichinari, Mitsuhiro; Oba, Katsuaki; Hattai, Takayuki; Takahashi, Toshio

PATENT ASSIGNEE(S): Shionogi and Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 25 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

Updated Search

SearchSTN

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 63227552	A	19880921	JP 1987-59560	19870313
PRIORITY APPLN. INFO.:			JP 1987-59560	19870313

OTHER SOURCE(S): MARPAT 111:153338

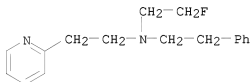
AB The title compds. R1R2NCH2CH2F (I) [R1 = (substituted) Ph, phenylalkyl, pyridyl, etc.; R2 = H, alkyl, haloalkyl, alkanoylalkyl, etc.; or R1R2 = carbazole, (substituted) phenothiazine, etc.; when R1 is substituted Ph, R2 is other than 2-fluoroethyl], useful as insecticides and microbicides, were prepared. A mixture of PhNH2 and BrCH2CH2F was heated at 60° for 19 h to give N-(2-fluoroethyl)aniline. A solution containing I (R1 = Ph, R2 = PhCH2CO) (concentration 500 ppm) gave 75% control of *Pseudoperonospora cubensis*.

IT 122975-04-6P

RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of, as insecticide, acaricide, and microbicide)

RN 122975-04-6 HCAPLUS

CN 2-Pyridineethanamine, N-(2-fluoroethyl)-N-(2-phenylethyl)- (CA INDEX NAME)



L16 ANSWER 41 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1989:478020 HCAPLUS

DOCUMENT NUMBER: 111:78020

ORIGINAL REFERENCE NO.: 111:13155a,13158a

TITLE: Preparation of pharmaceutically active heterocyclic amines and their use for treating head injury, spinal trauma, stroke, etc.

INVENTOR(S): McCall, John M.; Ayer, Donald E.; Jacobsen, E. Jon; Van Doornik, Frederick J.; Palmer, John R.

PATENT ASSIGNEE(S): Upjohn Co., USA

SOURCE: PCT Int. Appl., 173 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

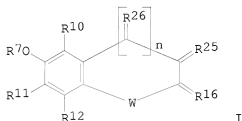
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8808424	A1	19881103	WO 1988-US1212	19880420
W: AU, DK, FI, JP, KR, NO, US				

Updated Search

SearchSTN

RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
CA 1338012	C	19960130	CA 1988-564335	19880415
EP 293078	A1	19881130	EP 1988-303576	19880420
R: ES, GR				
AU 8817098	A	19881202	AU 1988-17098	19880420
AU 624788	B2	19920625		
EP 358676	A1	19900321	EP 1988-904101	19880420
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 02503198	T	19901004	JP 1988-503777	19880420
JP 07103118	B	19951108		
EP 487510	A1	19920527	EP 1992-200013	19880420
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 5120843	A	19920609	US 1989-425726	19891023
DK 8905335	A	19891026	DK 1989-5335	19891026
PRIORITY APPLN. INFO.:			US 1987-43274	A2 19870427
			WO 1988-US1212	A 19880420
OTHER SOURCE(S):			MARPAT 111:78020	
GI				



AB The aromatic amines, alkylamines, bicyclic amines, cycloalkylamines, aromatic bicyclic amines, hydroquinoneamines, amino ethers, and bicyclic amino ethers, which are individually represented by Markush formula, e.g. bicyclic amines I [W = O, S, NH, C1-3 alkylimino; n = 0, 1, or 2; R7 = H, C1-4 alkyl, C1-4 alkyl, C1-4 alkylcarbonyl, PhCO, prodrug (e.g. PO2O-, COCH2CONHCH2SO2O-, or COCH:CHCO2-); R10 - R12 = H, Me; when R25 = R26 = H, R16 = α -R17: β -R18 where one of R17 and R18 = H, Me, Et, or Ph and the other is COM (M = substituted NH2, heterocyclic amino; or C:CON:NCQ:CH where Q = 2-pyridinyl), (CH2)pCOM (p = 1-6), (CH2)qM (q = 1-6) or CO2(CH2)rM (r = 2-6); when n = 0, R16 = R19:R20 where one of R19 and R20 taken together with R25 forms a second bond between the C atoms to which R16 and R25 are attached and the other = M-substituted groups described for R16; when n = 1, R25R26 = bond between the C atoms to which R25 and R26 are attached; the original Markush definition was not completed.], useful as pharmaceuticals for treatment of head injury, spinal trauma, stroke and a number of other related injuries and conditions (no data), are prepared A mixture of 6-bromohexanol, 2,6-bis(1-pyrrolidinyl)-4-(1-piperazinyl)-1,3,5-triazine, K2CO3, and NaI in MeCN was refluxed to give 4-[4,6-bis(1-pyrrolidinyl)-1,3,5-triazin-2-yl]-1-piperazinehexanol.

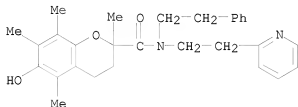
IT 122003-35-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, for treatment of head injury and spinal trauma and stroke)

SearchSTN

RN 122003-35-4 HCAPLUS

CN 2H-1-Benzopyran-2-carboxamide, 3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-N-(2-phenylethyl)-N-[2-(2-pyridinyl)ethyl]- (CA INDEX NAME)



L16 ANSWER 42 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1988:473335 HCAPLUS

DOCUMENT NUMBER: 109:73335

ORIGINAL REFERENCE NO.: 109:12281a,12284a

TITLE: Pyridineethanolamine derivatives, procedure for their preparation, and their use in treating obesity, diabetes mellitus, and increased protein degradation

INVENTOR(S): Alig, Leo; Muller, Marcel

PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Switz.

SOURCE: Eur. Pat. Appl., 16 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 254856	A2	19880203	EP 1987-108706	19870616
EP 254856	A3	19890208		
EP 254856	B1	19910904		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
CA 1287061	C	19910730	CA 1987-538235	19870528
US 4800206	A	19890124	US 1987-57150	19870603
FI 8702589	A	19871228	FI 1987-2589	19870610
AT 66916	T	19910915	AT 1987-108706	19870616
ES 2038619	T3	19930801	ES 1987-108706	19870616
ZA 8704449	A	19880224	ZA 1987-4449	19870619
AU 8774557	A	19880107	AU 1987-74557	19870622
AU 594788	B2	19900315		
IL 82945	A	19910610	IL 1987-82945	19870622
HU 44508	A2	19880328	HU 1987-2860	19870624
HU 198457	B	19891030		
DK 8703295	A	19871228	DK 1987-3295	19870626
DK 166207	B	19930322		
DK 166207	C	19930816		
NO 8702701	A	19871228	NO 1987-2701	19870626
NO 170973	B	19920928		
NO 170973	C	19930106		
JP 63008374	A	19880114	JP 1987-157957	19870626

SearchSTN

US 4988714
PRIORITY APPLN. INFO.:

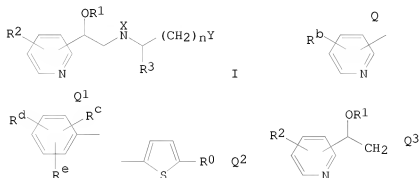
A 19910129

US 1988-236802
CH 1986-2608
CH 1987-1186
US 1987-57150
EP 1987-108706

19880826
A 19860627
A 19870327
A3 19870603
A 19870616

OTHER SOURCE(S): MARPAT 109:73335

GI



AB Pyridineethanolamines I [n = 1, 2; X = H, alkyl, alkoxyalkyl, CH₂CH₂ORa; Z = Q, Q1, 4-RfC₆H₄OCH₂; Y = 4-RC₆H₄, Q2; Ro = alkyl, COR4, CR5:CHCOR4; R = Ro, R'; R'' = H, alkyl, alkanoyl, (CH₂)₁-6OH, (CH₂)₁-6O(CH₂)₁-6R₆, (CH₂)₁-6COR4; R1, Ra = alkanoyl, Bz, (CH₂)₁-6 OH; R2, Rb = H, Cl, Br, CF₃; R3, R5 = H, Me; R4 = OH, alkoxy, NR7R8; R6 = H, Rg, OH, COR4; R7, R8 = H, alkyl; Rc, Re = H, Cl, F, Br, CF₃; Rd = H, NH₂; Rf = H, alkyl; Rg, Re = H, Cl, F, Br, CF₃; Rd = H, NH₂; Rf = H, AcNH, H₂NCOCH₂, R9CH₂CH₂OCH₂CH₂O; Rg, R9 = Ph (un)substituted with Cl, F, Br], useful in treating obesity, diabetes mellitus, and conditions with elevated protein degradation and as feed additives for fattened animals, were prepared by 2 methods: a) alkylation of X1X2NCHR3(CH₂)nY (1 of X1 and X2 = H, the other = X or Q3) with an agent introducing the group Qc or 1 of group X; and b) optionally functionally changing a reactive substituent in a group Y of the reaction product, optionally esterifying an OH β to the amine N atom, and optional conversion of I into a salt. Methylenation of 6-chloro-2-pyridinecarboxaldehyde with Me₂S:CH₂ gave 2-chloro-6-epoxyethylpyridine which reacted with 4-[(R)-2-aminopropyl]phenol to give α,α'-[[[(R)-4-hydroxy-α-methylphenethyl]imino]dimethylen e]bis[(RS)-6-chloro-2-pyridinemethanol] (II) and the corresponding monopyridine compound. Treating II with MeSO₂OCH₂CH₂OEt gave the 4-(ethoxyethoxy) analog of II. The latter, at 0.1 μM/kg in rats, gave 165% and 122% O consumption in 1-3 h and 1-12 h, resp., compared with the pre-treatment period O consumption. A formulation comprised (RS)-6-chloro-α-[[[(R)-4-(2-ethoxyethoxy)-α-methylphenethyl]amino]methyl]-2-pyridinemethanol 250, lactose 200, corn starch 300, corn starch paste 50, Ca stearate 5, and Lactose 45 mg.

IT 115548-08-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of obesity, diabetes mellitus, and

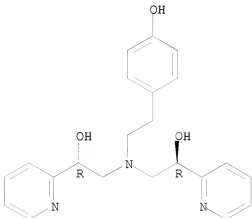
SearchSTN

elevated protein degradation remedy)

RN 115548-08-8 HCAPLUS

CN 2-Pyridinemethanol, α, α' -[[[2-(4-hydroxyphenyl)ethyl]imino]bis(methylene)]bis-, (R*,R*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L16 ANSWER 43 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1978:436894 HCAPLUS

DOCUMENT NUMBER: 89:36894

ORIGINAL REFERENCE NO.: 89:5615a,5618a

TITLE: Competitive and noncompetitive antagonism

AUTHOR(S): Van den Brink, Frans G.; Lien, Eric J.

CORPORATE SOURCE: USA

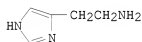
SOURCE: Handbuch der Experimentellen Pharmakologie (1978), 18(Histamine Anti-Histaminics, Part 2), 333-67

CODEN: HXPHAU; ISSN: 0073-0033

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

AB A comprehensive discussion is presented on the interactions of histamine (I) [51-45-6] agonists and antagonists with receptors. The pD2 value (the neg. logarithm of the molar concns. of the agonist which produces 50% of the maximum effect of the drug or receptors), pA2 value (neg. logarithm of the molar concns. of the antagonist in the presence of which twice the original concentration of the agonist is needed for the original effect), αE (intrinsic activity value), and pD21 value (the affinity to the metacoid receptors) for 75 drugs are given. These drugs react with the histaminergic system (guinea pig ileum) and also have an affinity for a cholinergic system (rat intestine). The effects of substitution of

Updated Search

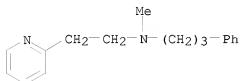
SearchSTN

various chemical groups on the receptor interactions of these drugs are also discussed.

IT 66711-31-7
 RL: PRP (Properties)
 (interaction of, with histamine receptors)

RN 66711-31-7 HCAPLUS

CN 2-Pyridineethanamine, N-methyl-N-(3-phenylpropyl)- (CA INDEX NAME)



L16 ANSWER 44 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1977:545548 HCAPLUS

DOCUMENT NUMBER: 87:145548

ORIGINAL REFERENCE NO.: 87:22929a,22932a

TITLE: pD2-, pA2- and pD2'-values of a series of compounds in a histaminic and a cholinergic system

AUTHOR(S): Van den Brink, Frans G.; Lien, Erik J.

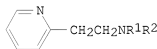
CORPORATE SOURCE: Dep. Pharmacol., Univ. Nijmegen, Nijmegen, Neth.

SOURCE: European Journal of Pharmacology (1977), 44(3), 251-70
 CODEN: EJPHAZ; ISSN: 0014-2999

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB Affinity and intrinsic activity values of 75 compds. for a histaminergic and a cholinergic system are presented. The quant. correlations between the affinity values of 35 derivs. of 2-(β-aminoethyl)pyridine (I) [2706-56-1] and some physicochem. consts. (Van der Waals volume, lipophilicity, number of hydrogen atoms on the protonated amine) are discussed. Absence of systematic differences between pD2 (agonist affinity) and pA2 (competitive antagonist affinity) of partial agonists supports the assumption that these values are equivalent expressions of the same affinity. The mimetic moiety in a number of the antihistaminic test compds. hardly contributes to their affinity. The affinity mainly depends on an interaction tendency with addnl. receptor areas. The correlation between pA2 and pD2' (affinity with respect to metacoid (noncompetitive) receptors) of the whole series of compds. in the histaminergic system is artificial. The method only allows determination of both values if their ratio lies between certain limits. The correlation between pA2 and pD2' for 16 closely related compds. in the guinea pig ileum and for nearly all compds. in the rat intestine has to be explained by an influence of the structural

differences on drug transference and/or the less specific binding forces. The metacoid receptors in the 2 systems are different structures. Possible mol. modifications to maximize the separation of antihistaminic from cholinergic affinity are suggested.

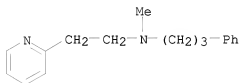
IT 64335-19-9

RL: BIOL (Biological study)

(cholinergic and histaminergic receptors affinity to, agonist and antagonist activity in)

RN 64335-19-9 HCAPLUS

CN 2-Pyridineethanamine, N-methyl-N-(3-phenylpropyl)-, dihydrobromide (9CI)
(CA INDEX NAME)



● 2 HBr

L16 ANSWER 45 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1971:125432 HCAPLUS

DOCUMENT NUMBER: 74:125432

ORIGINAL REFERENCE NO.: 74:20259a,20262a

TITLE: Di-2-(2-pyridyl)-ethylamine derivatives

INVENTOR(S): Tachikawa, Ryuji; Miyatera, Tetsuo; Kawano, Yoichi;
Takagi, Hiroshi

PATENT ASSIGNEE(S): Sankyo Co., Ltd.

SOURCE: Jpn. Tokkyo Koho, 3 pp.

CODEN: JAXXAD

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GI	JP 46003578	B4	19710128	JP	19670329

AB For diagram(s), see printed CA Issue.

of I, useful as an antitussive, local anesthetic, and uterus tonica, is manufactured by treating 2-vinylpyridine (II) with a primary amine. A mixture of 19.2 g II, 7.45 g NH₂Et.HCl, 25 ml MeOH, and 5.4 g AcOH is refluxed 8 hr, evaporated, small amount of ice-H₂O added to the residue, the mixture made strongly alkaline, and extracted with Et₂O to give 20 g I (R = Et), b₅ 150-60°. Similarly prepared are I (R and b.p./mm given): p-ClC₆H₄CH₂, 175-85°/0.01-0.001; 2-(1-piperidyl)-ethyl, 190-200°/760; 3-(N,N-diethylamino)propyl, 210-20°/0.1; 3-morpholinopropyl, 180-90°/0.05; iso-Bu, 180°/0.06; allyl, 138-42°/0.09; PhCH₂, 180°/0.05; phenethyl,

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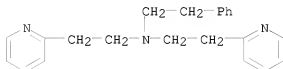
193-7°/0.4; 2-(N,N-dibutylamino)ethyl, 155-60°/0.01-0.001;
3,4-dimethoxybenzyl, 225-30°/0.2.

IT 31582-30-6P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 31582-30-6 HCAPLUS

CN 2-Pyridineethanamine, N-(2-phenylethyl)-N-[2-(2-pyridinyl)ethyl]- (CA
INDEX NAME)



L16 ANSWER 46 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1961:50002 HCAPLUS

DOCUMENT NUMBER: 55:50002

ORIGINAL REFERENCE NO.: 55:9666d-e

TITLE: Autonomic drugs and their receptors

AUTHOR(S): Ariens, E. J.; Simonis, A. M.

CORPORATE SOURCE: Univ. Nijmegen, Neth.

SOURCE: Archives Internationales de Pharmacodynamie et de
Therapie (1960), 127, 479-96
CODEN: AIPTAK; ISSN: 0003-9780

DOCUMENT TYPE: Journal

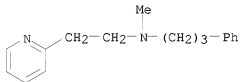
LANGUAGE: English

AB The relations between structure and activity in various series of
autonomic drugs and of histamine were studied. In regard to
sympathomimetic agents it is concluded that the α -mimetic effects
particularly involve interaction with the amino group structure, whereas
for the β -mimetic effects the interaction of the catechol nucleus of
the mol. is essential.

IT 66711-31-7, Pyridine, 2-[2-[methyl(3-phenylpropyl)amino]ethyl]-
(biol. activity of)

RN 66711-31-7 HCAPLUS

CN 2-Pyridineethanamine, N-methyl-N-(3-phenylpropyl)- (CA INDEX NAME)



L16 ANSWER 47 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1957:77178 HCAPLUS

DOCUMENT NUMBER: 51:77178

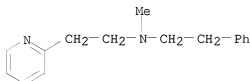
ORIGINAL REFERENCE NO.: 51:13941f-i, 13942a

TITLE: Dimethylaminopropylidipyrithiazane

SearchSTN

INVENTOR(S): Rath, Stephen
 DOCUMENT TYPE: Patent
 LANGUAGE: Unavailable
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	US 2789978		19570423	US 1954-443690	19540715
GI	For diagram(s), see printed CA Issue.				
AB	The preparation of I where X is Se or S and Z is CH or N is described. E.g., 75 g. phenoselenazine, 15 g. NaNH ₂ , and 250 g. xylene was heated to reflux and 55 g. 1-diethylamino-2-chloropropane in 55 g. xylene added in 1 hr., the mixture refluxed for another hr., cooled, mixed with 800 g. H ₂ O, and acidified with dilute HCl. The aqueous layer was separated, made strongly alkaline with aqueous NaOH, and finally extracted with ether. Evaporation of the ether gave a mixture of N-(2-diethylamino-2-methylethyl)phenoselenazine (I) and N'-(2-diethylamino-1-methylethyl)phenoselenazine (II). The HCl salts of I and II were precipitated from EtOAc by the addition of dry HCl gas and were fractionally crystallized from alc. (I HCl salt crystallizes first). The preparation of the following compds. is also described (no phys. properties given): N-(3-dimethylaminopropyl)phenoselenazine HCl salt, N-(3-dimethylaminopropyl)-2-chlorophenoselenazine HCl salt, N-(3-dimethylaminopropyl)phenoselenazine oxide HCl salt, N-(3-dimethylaminopropyl) phenothiazine-2-sulfonic acid sulfate, N-(3-dimethylaminopropyl)phenothiazine-2-carboxylic acid sulfate, N-(3-carboxamidopropyl)-2-chlorophenothiazine HCl salt, N-(3-carboxamido-1-carboxypropyl)-2-chlorophenothiazine HCl salt, N-[1,3-(dimethylamino)-2-propyl]phenothiazine HCl salt, N-(3-dimethylaminopropyl)-p-thiazine, N-(3-dimethylaminopropyl)dipyridothiazine, N-(3-dimethylaminopropyl)-2,4-dinitrophenothiazine, and N-(3-dimethylaminopropyl)-2-nitroselenazine.				
IT	110424-58-3P, Pyridine, 2-[2-(methylphenethylamino)ethyl]-, dihydrochloride RL: PREP (Preparation of (preparation of)				
RN	110424-58-3 HCAPLUS				
CN	Pyridine, 2-[2-(methylphenethylamino)ethyl]-, dihydrochloride (6CI) (CA INDEX NAME)				

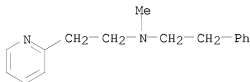


● 2 HCl

SearchSTN

L16 ANSWER 48 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 1957:77177 HCAPLUS
 DOCUMENT NUMBER: 51:77177
 ORIGINAL REFERENCE NO.: 51:13941f
 TITLE: 2-Pyridylethylphenylethylalkylamines
 INVENTOR(S): Blicke, Frederick F.
 PATENT ASSIGNEE(S): University of Michigan
 DOCUMENT TYPE: Patent
 LANGUAGE: Unavailable
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	US 2792403		19570514	US 1955-480063	19550105
AB	A mixture of 9.2 parts MeNHCH ₂ CH ₂ Ph and 10.5 parts 2-vinylpyridine was refluxed 5 hrs. and distilled to give 2-C ₅ H ₄ NCH ₂ CH ₂ NMeCH ₂ CH ₂ Ph, b ₁₅ 197-200°; HCl salt, m. 157-8° (from ethanol-ether). Compds. of this type have adrenolytic activity and blood pressure-lowering effect.				
IT	110424-58-3P, Pyridine, 2-[2-(methylphenethylamino)ethyl]-, dihydrochloride				
	RL: PREP (Preparation) (preparation of)				
RN	110424-58-3 HCAPLUS				
CN	Pyridine, 2-[2-(methylphenethylamino)ethyl]-, dihydrochloride (6CI) (CA INDEX NAME)				



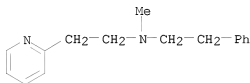
●2 HCl

L16 ANSWER 49 OF 49 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 1957:77176 HCAPLUS
 DOCUMENT NUMBER: 51:77176
 ORIGINAL REFERENCE NO.: 51:13941d-f
 TITLE: Alkylpyridines
 INVENTOR(S): Cislak, Francis E.; Wheeler, Wm. R.
 PATENT ASSIGNEE(S): Reilly Tar & Chemical Corp.
 DOCUMENT TYPE: Patent
 LANGUAGE: Unavailable
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	US 2786846		19570326	US 1953-358953	19530601

SearchSTN

- AB 2- or 4-Alkylpyridines, where the alkyl group contains more than 1 C atom, are obtained by the vapor phase reaction of 2- or 4-picoline or alkylpicoline with an aliphatic aldehyde in the presence of Al₂O₃ (I) at 400-550°. Thus, passing a vaporized mixture of 1 mole each of 2-picoline and H₂CO through a fluidized bed of finely divided I (<100 mesh) at 450° with a superficial velocity of about 0.9 ft./sec. gives a high yield of 2-ethylpyridine and a smaller yield of 2-vinylpyridine (II). At lower temps., particularly when ZnF₂ is added to I, the formation of II predominates.
- IT 110424-58-3P, Pyridine, 2-[2-(methylphenethylamino)ethyl]-, dihydrochloride
 RL: PREP (Preparation)
 (preparation of)
- RN 110424-58-3 HCAPLUS
- CN Pyridine, 2-[2-(methylphenethylamino)ethyl]-, dihydrochloride (6CI) (CA INDEX NAME)



●2 HCl

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